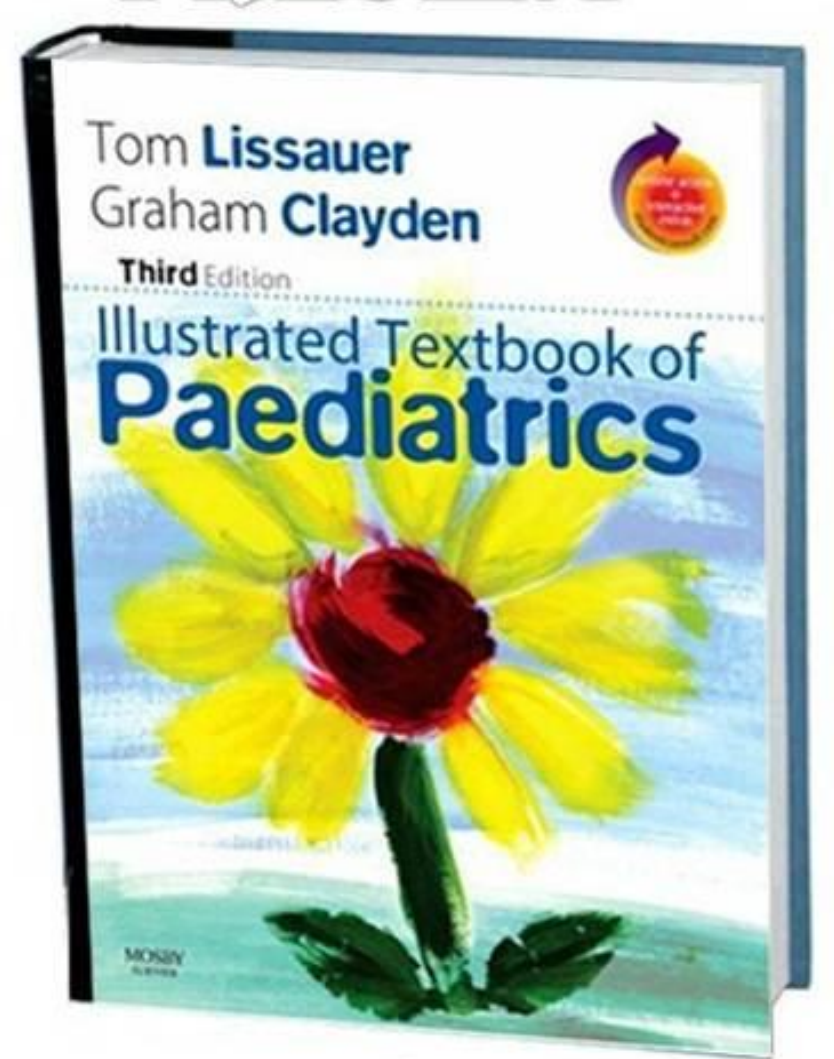


PRESENT



Lissauer's Extra Topics In Pediatrics

الموضوعات التي لم ترد في كتاب د/ مصطفي زكريا الجديد

MAINLY FOR MCQ

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Tonsillectomy and Adenoidectomy

Children with recurrent URTIs are often referred for removal of their tonsils and adenoids, one of the commonest operations performed in children. Many children have large tonsils but this in itself is not an indication for tonsillectomy as they shrink spontaneously in late childhood.

The indications for tonsillectomy are controversial but include:

- recurrent tonsillitis (as opposed to recurrent URTIs) - tonsillectomy reduces the number of episodes of tonsillitis by a third, e.g. from three to two per year
- a peritonsillar abscess (quinsy)
- obstructive sleep apnoea.

Like the tonsils, adenoids increase in size until about the age of 8 years and then gradually regress. In young children the adenoids grow proportionately faster than the airway, so that their effect of narrowing the airway lumen is greatest between 2 and 8 years of age. They may narrow the posterior nasal space sufficiently to justify adenoidectomy.

Indications for the removal of both the tonsils and adenoids are controversial but include:

- otitis media with effusion with hearing loss, when it gives a small additional benefit to the insertion of grommets (ventilation tubes).
- obstructive sleep apnoea (an absolute indication).

Sleep-Disordered Breathing

Up to 10% of children will snore, but less than 1% will have sleep-disordered breathing. Obstructive sleep apnoea (OSA) in childhood is usually due to upper airway obstruction secondary to adeno-tonsillar hypertrophy. There may be a history of loud snoring, apnoea for 30-45 seconds with struggling for breath, and disturbed sleep. Whilst affected children may be obese, others may have growth failure and they may have daytime hyperactivity rather than sleepiness. Overnight sleep studies show intermittent hypoxia and hyper-carbia. Adeno-tonsillectomy is usually curative

It is now recognised that children with a range of disorders may be prone to sleep-disordered breathing, particularly those with craniofacial disorders (e.g. Pierre Robin), neuromuscular disorders (e.g. muscular dystrophy) or hypotonia (e.g. Down's syndrome). There may be a mixture of obstructive and central hypoventilation. Many improve with overnight ventilation at home via a nasal mask.

Laryngeal & Tracheal Infections :

acute upper airways obstruction. They are characterised by:

- stridor, a rasping sound heard predominantly on inspiration
- hoarseness due to inflammation of the vocal cords
- a barking cough like a sea lion
- a variable degree of dyspnoea.

Differential diagnosis of acute upper airways obstruction

Croup

- Viral laryngotracheitis (very common)
- Acute-on-chronic stridor, e.g. from a floppy larynx (laryngomalacia)
- Bacterial tracheitis (rare)

Rare causes

- Epiglottitis
- Inhalation of smoke and hot air in fires
- Trauma to the throat
- Retropharyngeal abscess
- Laryngeal foreign body
- Allergic laryngeal oedema (angioedema)
- Tetany due to poor vitamin D intake
- Infectious mononucleosis
- Measles
- Diphtheria

ASTHMA

CLINICAL FEATURES ACUTE ATTACK, :

- Wheeze and tachypnoea (respiratory rate >50 breaths/min in children 2-5 years, >30 breaths/min in children 5 or over) - but poor guide to severity.
- Increasing tachycardia (>130 beats/min in children aged 2-5 years, >120 beats/min in children 5 or over) - better guide to severity.
- The use of accessory muscles and chest recession - also better guide to severity.
- The presence of marked pulsus paradoxus (the difference between systolic pressure on inspiration and expiration) indicates moderate to severe in children but is difficult to measure accurately and is therefore unreliable.
- If breathlessness interferes with talking, the attack is severe.
- Cyanosis, fatigue and drowsiness are late signs, indicating life-threatening asthma; this may be accompanied by a silent chest on auscultation as little air is being exchanged.

However, the severity of an acute asthma may be underestimated by clinical examination alone. Therefore:

- Arterial oxygen saturation should be measured with a pulse oximeter in all children presenting to hospital with acute asthma. Oxygen saturations <92% in air imply severe or life-threatening asthma.
- Measurement of the peak expiratory flow rate should be routine in school-age children.

choosing the correct inhaler

Inhaled drugs may be administered via a variety of devices, chosen according to the child's age and preference:

- metered dose inhaler
- breath-actuated metered dose inhaler, e.g. Autohaler or Easi-Breathe
- dry powder devices, e.g. terbutaline sulphate (Bricanyl Turbohaler) and

salbutamol (Ventolin Accuhaler).

The pressurised metered-dose inhaler (MDI) requires the greatest coordination and should never be used alone in children. Using an MDI through a spacer device such as the Nebuhaler or aerochamber significantly increases the proportion of the drug reaching the airways, reduces impaction of drug on the throat and requires less coordination. In young children, a soft face mask can be attached to the spacer Fig. 16.15. Ideally inhaled steroids should always be given by MDI and spacer, and spacers should be used in young children and for delivering beta agonists during acute asthma attacks. Spacers are very effective at delivering bronchodilators and inhaled steroids to the preschool child.

Breath-actuated devices and dry-powder inhalers require less coordination than MDIs and can be used for delivering beta agonists in school-age children.

Nebulised treatment is now only given for severe life-threatening asthma, or rarely for children who need inhaled therapy but are unable to use any of these devices or require high dose

Criteria for hospital admission

Children require hospital admission if, after high-dose inhaled bronchodilator therapy, they:

- have not responded adequately clinically - persisting breathlessness, tachypnoea
- are exhausted
- still have a marked reduction in their predicted (or usual) peak flow rate
- have a reduced oxygen saturation (<92% in air).

Chronic Lung Infection

Children with recurrent pneumonia or who produce purulent sputum may have bronchiectasis, which is permanent dilatation of the bronchi.

It is helpful to determine if recurrent pneumonia affects different lobes of the lung (generalised), or only one lobe (focal). Generalised causes include cystic fibrosis, primary ciliary dyskinesia, immunodeficiency or chronic aspiration. Bronchiectasis following severe pneumonia, particularly tuberculosis, pertussis or measles, has now become uncommon. Although a plain chest X-ray may show gross bronchiectasis, it is best seen on a CT scan of the chest

Cystic fibrosis is considered below. In primary ciliary dyskinesia, the microcilia of the respiratory epithelium, which are an important defence against infection, are abnormal in structure or function. Affected children have recurrent infection of the upper and lower respiratory tract. They characteristically have recurrent productive cough, a purulent nasal discharge and chronic ear infections; 50% also have dextrocardia and situs inversus (Kartagener's syndrome). Ciliary structure can be assessed by electron microscopy of nasal mucosal brushings.

Children with immunodeficiency may develop severe, unusual or recurrent chest infections. The immune deficiency may be secondary to an illness, e.g. malignant disease or its treatment with chemotherapy. Less commonly it is due to HIV infection or a primary immune deficiency.

Many neurologically impaired children will have chronic aspiration, either due to oropharyngeal incoordination or due to gastro-oesophageal reflux.

Tuberculosis remains an important cause of chronic lung infection and all children with a persistent productive cough should have a chest X-ray and tuberculin skin test. Marked hilar or paratracheal lymphadenopathy is highly suggestive of tuberculosis.

Cardiac disorders

CIRCULATORY CHANGES AT BIRTH

In the fetus, the left atrial pressure is low, as relatively little blood returns from the lungs. The pressure in the right atrium is higher than in the left, as it receives all the systemic venous return including blood from the placenta. The flap valve of the foramen ovale is held open, blood flows across the atrial septum into the left atrium and then into the left ventricle, which in turn pumps it to the upper body

With the first breaths, resistance to pulmonary blood flow falls and the volume of blood flowing through the lungs increases sixfold. This results in a rise in the left atrial pressure. Meanwhile, the volume of blood returning to the right atrium falls as the placenta is excluded from the circulation. The change in the pressure difference causes the flap valve of the foramen ovale to be closed. The ductus arteriosus, which connects the pulmonary artery to the aorta in fetal life, will normally close within the first few hours or days. Some babies with congenital heart lesions rely on blood flow through the duct (duct-dependent circulation). Their clinical condition will deteriorate dramatically when the duct closes, which is usually at 1-2 days of age but occasionally later

CAUSES OF CONGENITAL HEART DISEASE

	Cardiac abnormalities	Frequency
Maternal disorders		
Rubella infection	Peripheral pulmonary stenosis, PDA	30-35%
Systemic lupus erythematosus (SLE)	Complete heart block (anti-Ro and anti-La antibody)	35%
Diabetes mellitus	Incidence increased overall	2%
Maternal drugs		
Warfarin therapy	Pulmonary valve stenosis, PDA	5%
Fetal alcohol syndrome	ASD, VSD, tetralogy of Fallot	25%
Chromosomal abnormality		
Down's syndrome (trisomy 21)	Atrioventricular septal defect, VSD	30%
Edwards' syndrome (trisomy 18),	Complex	60-80%
Patau's syndrome (trisomy 13)		
Turner's syndrome (45XO)	Aortic valve stenosis, coarctation of the aorta	15%
Chromosome 22q11.2 deletion	Aortic arch anomalies, tetralogy of Fallot	
Williams' syndrome (chromosome 7 microdeletion)	Supravalvular aortic stenosis, peripheral pulmonary artery stenosis	

The features of an innocent murmur can be remembered as the five S's:InnoSent murmur = Soft, Systolic, aSymptomatic, left Sternal edge

Congenital heart disease presents with:

- antenatal ultrasound screening - increasing proportion detected
- detection of a heart murmur - need to differentiate innocent from pathological murmur
- cyanosis - if duct dependent, prostaglandin to maintain ductal patency is vital for initial survival

- heart failure - usually from left-to-right shunt when pulmonary vascular resistance falls, in neonate from left heart obstruction
- shock - when duct closes in severe left heart obstruction

Summary

LEFT-TO-RIGHT SHUNTS

Lesion	Symptoms	Signs	Management
ASD - secundum	None	Ejection systolic murmur at ULSE	Catheter device closure at 3-5 years
AVSD - partial	None, heart failure	Fixed split S2	Surgery at 3 years
VSD - small (80-90%)	None	Pansystolic murmur at LLSE	None
VSD - large (10-20%)	Heart failure	Active precordium, loud P2, soft murmur, tachypnoea, hepatomegaly	Diuretics, captopril , calories Surgery at 3-6 months old
PDA - term	None	Continuous murmur at ULSE ± bounding pulses	Coil or device closure at cardiac catheter
PDA - preterm	None, heart failure	Systolic murmur at ULSE ± bounding pulses	Fluid restriction, indomethacin or ibuprofen , or surgical ligation

HYPOPLASTIC LEFT HEART SYNDROME

In this condition there is underdevelopment of the entire left side of the heart. The mitral valve is small or atretic, the left ventricle is diminutive and there is usually aortic valve atresia. The ascending aorta is very small, and there is almost invariably coarctation of the aorta.

Clinical features

These children may be detected antenatally at ultrasound screening. This allows for effective counselling and prevents the child from becoming sick after birth.

- If they do present after birth, they are the sickest of all neonates presenting with a duct-dependent systemic circulation.
- There is no flow through the left side of the heart, so ductal constriction leads to profound acidosis and rapid cardiovascular collapse.
- There is weakness or absence of all peripheral pulses, in contrast to weak femoral pulses in coarctation of the aorta.

Diagnosis :

- Hyperoxia test : The infant will fail the hyperoxia (nitrogen washout) test by remaining desaturated in oxygen, as there is common mixing of pulmonary venous and systemic venous blood at atrial level.
- As in all suspected duct-dependent lesions, prostaglandin must be commenced
- the diagnosis established urgently by echocardiography.

Management

The management of this condition consists of a difficult neonatal operation called the Norwood procedure. This is followed by a further operation (Glenn or hemi-Fontan) at about 6 months and again (Fontan) at about 3 years.

Summary

Left heart outflow obstruction in the sick infant - duct-dependent lesions

Lesion	Clinical features	Management
Coarctation of the aorta and interruption of the aortic arch	Heart murmur, heart failure Circulatory collapse Weak or absent femoral pulses Blood pressure arms > legs	Maintain airway, breathing, circulation Immediately start prostaglandin infusion

Hypoplastic left heart syndrome	Circulatory collapse All peripheral pulses weak or absent	Maintain airway, breathing, circulation Immediately start prostaglandin infusion surgery)

MANAGEMENT OF FALLOT TETROLOGY

Initial management is medical, with corrective surgery at around 6 months of age. It involves closing the VSD and relieving right ventricular outflow tract obstruction with an artificial patch, which sometimes extends across the pulmonary valve. Most are free from significant symptoms in childhood.

Infants who are very cyanosed in the neonatal period require a shunt to increase pulmonary blood flow. This is usually done by surgical placement of an artificial tube between the subclavian artery and the pulmonary artery (a modified Blalock-Taussig shunt) or sometimes by balloon dilatation of the right ventricular outflow tract.

Hypercyanotic spells are usually self-limiting and followed by a period of sleep. If prolonged (beyond about 15 minutes), they require prompt treatment with:

- sedation and pain relief (morphine is excellent)
- intravenous propranolol (or an alpha adrenoceptor agonist), which probably works both as a peripheral vasoconstrictor and by relieving the subpulmonary muscular obstruction that is the cause of reduced pulmonary blood flow
- intravenous volume administration
- bicarbonate to correct acidosis
- muscle paralysis and artificial ventilation in order to reduce metabolic oxygen demand.

MANAGEMENT OF TGA

In the sick cyanosed neonate, the key is to improve mixing of saturated and desaturated blood.

- **Maintaining the patency of the ductus arteriosus** with a prostaglandin infusion is mandatory
- **A balloon atrial septostomy** is a life-saving procedure which may be performed in children with any form of transposition of the great arteries. A catheter, with an expandable balloon at its tip, is passed through the umbilical or femoral vein and then on through the right atrium and foramen ovale. The balloon is inflated within the left atrium and then pulled through the atrial septum. This tears the atrial septum, renders the flap valve of the foramen ovale incompetent, and so allows mixing of the systemic and pulmonary venous blood within the atrium.

All patients with transposition of the great arteries will require surgery, which is usually **the arterial switch procedure**. In this operation, performed in the first few days of life, the pulmonary artery and aorta are transected above the arterial valves and switched over. In addition, the coronary arteries have to be transferred across to the new aorta. Thus the left ventricle acts as the systemic ventricle, pumping fully oxygenated blood into the aorta, and the right ventricle assumes its more normal role of pumping blood to the lungs,

TRICUSPID ATRESIA

In tricuspid atresia only the left ven-tricle is effective, the right being small and non-functional

Clinical features

There is 'common mixing' of systemic and pulmonary venous return in the left atrium. Presentation is with cyanosis in the newborn period if duct-dependent, or the child may be well at birth and become cyanosed or breathless.

Management

Early palliation is performed to maintain a secure supply of blood to the lungs at low pressure, by:

- a Blalock-Taussig shunt (between the subclavian and pulmonary artery) in children who are severely cyanosed
- pulmonary artery banding to reduce pulmonary blood flow if breathless.

Completely corrective surgery is not possible as there is only one effective functioning ventricle. Palliation is performed (Glenn or hemi-Fontan operation connecting the superior vena cava to the pulmonary artery after 6 months of age and

a Fontan operation to also connect the inferior vena cava to the pulmonary artery at 3-5 years).
Thus the left ventricle drives blood around the body and systemic venous pressure supplies blood to the lungs. The Fontan operation results in a less than ideal functional outcome, but has the advantages of relieving cyanosis and removing the long-term volume load on the single functional ventricle

Hematological disorders

HEMOLYTIC ANEMIA

Haemolysis from increased red cell breakdown leads to:

- anaemia
- reticuloendothelial hyperplasia - hepatomegaly and splenomegaly
- elevated unconjugated bilirubin
- excess urinary urobilinogen.

The diagnostic clues to haemolysis are:

- raised reticulocyte count (on the blood film this is called 'polychromasia' as the reticulocytes have a characteristic lilac colour)
- unconjugated bilirubinaemia and increased urinary urobilinogen
- abnormal appearance of the red cells on a blood film (e.g. spherocytes, sickle shaped or very hypochromic) (Fig. 22.6)
- positive direct antiglobulin test (only if an immune cause as this test identifies antibody-coated red blood cells)
- increased erythropoiesis in the bone marrow.

SICKLE CELL ANEMIA

Management

PROPHYLAXIS

1-In order to prevent pneumococcal infection,
- all patients should receive twice daily penicillin throughout childhood and
- be immunised against pneumococcus. The child should be fully immunised, including against *Haemophilus influenzae* type b.

2-All patients should receive once daily oral folic acid because of the increased demand for folic acid caused by the chronic haemolytic anaemia.
3- Vaso-occlusive crises should be minimised by avoiding exposure to cold, dehydration, excessive exercise, undue stress or hypoxia. This requires common sense measures –
- dressing children warmly,
- giving drink especially before exercise
- and taking extra care to keep children warm after swimming or when playing outside in the winter.

TREATMENT OF ACUTE CRISES

Painful crises should be treated with
- oral or intravenous analgesia according to need (may require opiates) and
- good hydration (oral or intravenous as required);
- infection should be treated with antibiotics;
- oxygen should be given if the oxygen saturation is reduced.
- Exchange transfusion is indicated for acute chest syndrome, stroke and priapism.

TREATMENT OF CHRONIC PROBLEMS

1-- Children who have recurrent hospital admissions for painful vaso-occlusive crises or acute chest syndrome

may benefit *from hydroxyurea* , a drug which increases their HbF production and helps protect against further crises. It requires monitoring for side-effects.

2-- The most severely affected children (1-5%) who have had a stroke or who do not respond to hydroxyurea may be offered *a bone marrow transplant*. This is the only cure for sickle cell disease but can only be safely carried out if the child has an HLA-identical sibling who can donate their bone marrow - the cure rate is 90% but there is a 5% risk of fatal transplant-related complications.

Prognosis

Sickle cell disease is a cause of premature death due to one or more of these severe complications; around 50% of patients with the most severe form of sickle cell disease die before the age of 40 years. However, the mortality rate during childhood is around 3%, usually from bacterial infection.

Prenatal diagnosis and screening

Many countries with a high prevalence of haemoglobinopathies, including the UK, perform neonatal screening using the biochemical screening test (Guthrie test). Early diagnosis of sickle cell disease allows penicillin prophylaxis to be started in early infancy instead of awaiting clinical presentation, possibly due to a severe infection. Prenatal diagnosis can be carried out by chorionic villus sampling at the end of the first trimester if parents wish to choose this option to prevent the birth of an affected child.

ANAEMIA IN THE NEWBORN

1. Reduced red blood cell production

There are two main but rare causes in the newborn and both cause red cell aplasia:

- congenital infection with parvovirus B19
- congenital red cell aplasia (Diamond-Blackfan anaemia).

In this situation the Hb is low and the red blood cells look normal. The diagnostic clue is that the reticulocyte count is low and the bilirubin is normal.

2. Increased red cell destruction (haemolytic anaemia)

This occurs either because of an antibody destroying the red blood cells (i.e. an extrinsic cause) or because there is an intrinsic abnormality of the surface or intracellular contents of the red blood cell. The main causes of haemolytic anaemia in neonates are:

- immune (e.g. haemolytic disease of the newborn)
- red cell membrane disorders (e.g. hereditary spherocytosis)
- red cell enzyme disorders (e.g. glucose-6-phosphate dehydrogenase deficiency)
- abnormal haemoglobins (e.g. α-thalassaemia major).

The diagnostic clues to a haemolytic anaemia

are an increased reticulocyte count (due to increased red cell production to compensate for the anaemia) and increased unconjugated bilirubin (due to increased red cell destruction with release of this bile pigment into the plasma).

Haemolytic disease of the newborn (immune haemolytic anaemia of the newborn) is due to antibodies against blood group antigens. The most important are: anti-D (a 'Rhesus' antigen), anti-A or anti-B (ABO blood group antigens) and anti-Kell. The mother is always negative for the relevant antigen (e.g. rhesus D-negative) and the baby is always positive; the mother then makes antibodies against the baby's blood group and these antibodies cross the placenta into the baby's circulation causing fetal or neonatal haemolytic anaemia. The diagnostic clue to this type of haemolytic anaemia is a positive direct anti-globulin test (Coombs test). This test is only positive in antibody-mediated anaemias and so is negative in all the other types of haemolytic anaemia.

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The most common causes of non-immune haemolytic anaemia in neonates are: G6PD (glucose-6-phosphate dehydrogenase) deficiency and hereditary spherocytosis. Haemoglobinopathies, apart from α-thalassaemia, rarely present with clinical features in the neonatal period but are detected on neonatal biochemical screening (Guthrie test).

3. Blood loss

The main causes are:

- feto-maternal haemorrhage (occult bleeding into the mother)
- twin-to-twin transfusion (bleeding from one twin into the other one)
- blood loss around the time of delivery (e.g. placental abruption).

The main diagnostic clue is severe anaemia with a raised reticulocyte count and normal bilirubin.

4. Anaemia of prematurity

The main causes are:

- inadequate erythropoietin production
- reduced red cell lifespan
- frequent blood sampling whilst in hospital
- iron and folic acid deficiency (after 2-3 months).

Investigations in haemophilia A and von Willebrand's disease

	Haemophilia A	**von Willebrand's disease**
PT	Normal	Normal
APTT	↑↑	↑ or normal
Factor VIII:C	↓↓	↓ or normal
vWF Ag	Normal	↓
RiCoF (activity)	Normal	↓
Ristocetin-induced platelet aggregation	Normal	Abnormal
vWF multimers	Normal	Variable

Management of vWD

Treatment depends on the type and severity of the disorder.

- Type 1 vWD can usually be treated with DDAVP, which causes secretion of both FVIII and vWF into plasma. DDAVP should be used with caution in children <1 year of age as it can cause hyponatraemia due to water retention and may cause seizures, particularly after repeated doses and if fluid intake is not strictly regulated.
- More severe types of vWD have to be treated with *plasma-derived* FVIII concentrate as DDAVP is ineffective and recombinant FVIII concentrate contains no vWF.
- Cryoprecipitate is no longer used to treat vWD as it has not undergone viral inactivation.
- *Intramuscular injections, aspirin and non-steroidal anti-inflammatory drugs should be avoided in all patients with vWD.*

VOMITING

Diagnostic clues in a vomiting infant

- Bile-stained vomit - intestinal obstruction must be excluded
- Blood in the vomit - suggests oesophagitis or peptic ulceration or oral/nasal bleeding or malrotation
- Projectile vomiting in the first few weeks of life - is it pyloric stenosis?
- Are there symptoms to suggest urinary tract, central nervous system or gastrointestinal infection?
- Vomiting at the end of paroxysmal coughing - is it whooping cough (pertussis)?
- Is the infant dehydrated or in shock?
- Abdominal distension - is there lower intestinal obstruction? Check for a strangulated inguinal hernia.

PYLORIC STENOSIS

Diagnosis

- Unless immediate fluid resuscitation is required, a test feed is performed. The baby is given a milk feed, which will calm the hungry infant, allowing examination.
- Gastric peristalsis may be seen as a wave moving from left to right across the abdomen .
- The pyloric mass or 'olive' is usually palpable in the right upper quadrant. If the stomach is over distended with air, it will need to be emptied by a nasogastric tube to allow palpation.
- Ultrasound examination is used to confirm the diagnosis if no mass is felt.
- A barium meal is only performed when the diagnosis remains in doubt.

MECKEL'S DIVERTICULUM

Pathology :

Two per cent of individuals have an ileal remnant of the vitellointestinal duct, in the form of a Meckel's diverticulum, which contains ectopic gastric mucosa or pancreatic tissue.

Clinical presentation :

Most are asymptomatic but they may present with severe rectal bleeding which is neither bright red nor true melaena. Other forms of presentation include intussusception, volvulus around a band, or diverticulitis which mimics appendicitis.

Diagnosis :

A technetium scan will demonstrate increased uptake by ectopic gastric mucosa in 70% of cases.

Treatment :

is by surgical resection

MALROTATION

Pathology :

If the small bowel mesentery is not fixed at the duodenojejunal flexure or in the ileocaecal region, its base is shorter than normal, predisposing to volvulus. It may arise in the fetus from the duodenojejunal flexure failing to rotate adequately to the left around the superior mesenteric vessels or the caecum failing to rotate and descend on the right. Ladd's bands may cross the duodenum, contributing to an obstruction. The position of the superior mesenteric artery and vein relative to each other on abdominal ultrasound is helpful diagnostically.

Presentation :

There are two presentations:

- obstruction
- obstruction with a compromised blood supply.

If there is infarction of the bowel, blood may be seen in the gastric aspirates or in the stool. Obstruction with bilious vomiting usually presents in the first few days of life but can be seen at a later age.

Any child with dark green vomiting needs an upper gastrointestinal contrast study to assess intestinal rotation, unless signs of vascular compromise are present, when an urgent laparotomy is needed.

Treatment :

At operation, the volvulus is untwisted, the duodenum mobilised and the bowel placed in the non-rotated position with the duodenojejunal flexure on the right and the caecum and appendix on the left. The malrotation is not 'corrected', but the mesentery broadened. The appendix may be removed to avoid later diagnostic confusion in the event of appendicitis.

GASTRITIS AND PEPTIC ULCERATION

Aetiology :

The greater use of endoscopy in children and the identification of the Gram-negative organism *Helicobacter pylori* in association with antral gastritis have focused attention on it as a potential cause of abdominal pain in children. In adults, there is substantial evidence that *H. pylori* is a strong predisposing factor to duodenal ulcers. This association in children is much less clear. Duodenal ulcers are uncommon in children but should be sought in those with night pain, particularly if it wakes them, or when there is a history of peptic ulceration in a first-degree relative.

Clinical picture :

H. pylori causes a nodular antral gastritis which may be associated with abdominal pain and nausea.

Diagnosis :

- It is usually identified in gastric antral biopsies, but may also be present on micro-aerophilic culture. The organism produces urease, which forms the basis for a laboratory test on biopsies, and
- the ^{13}C breath test following the administration of ^{13}C-labelled urea by mouth.
- Serological tests are unreliable in children.

Treatment :

Treatment regimens vary but often consist of triple therapy with, for example, amoxicillin , metronidazole and clarithromycin .

POST-GASTROENTERITIS SYNDROME

Pathology :

Infrequently, following an episode of gastroenteritis, the introduction of a normal diet results in a return of watery diarrhoea. Temporary lactose intolerance may have developed,

Diagnossi :

which can be confirmed by the presence of non-absorbed sugar in the stools giving a positive Clinitest result.

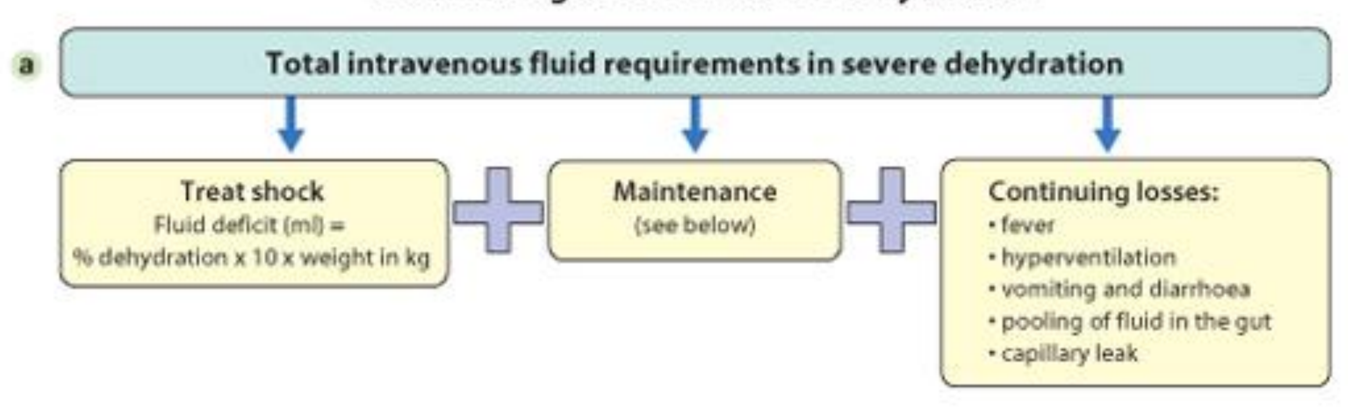
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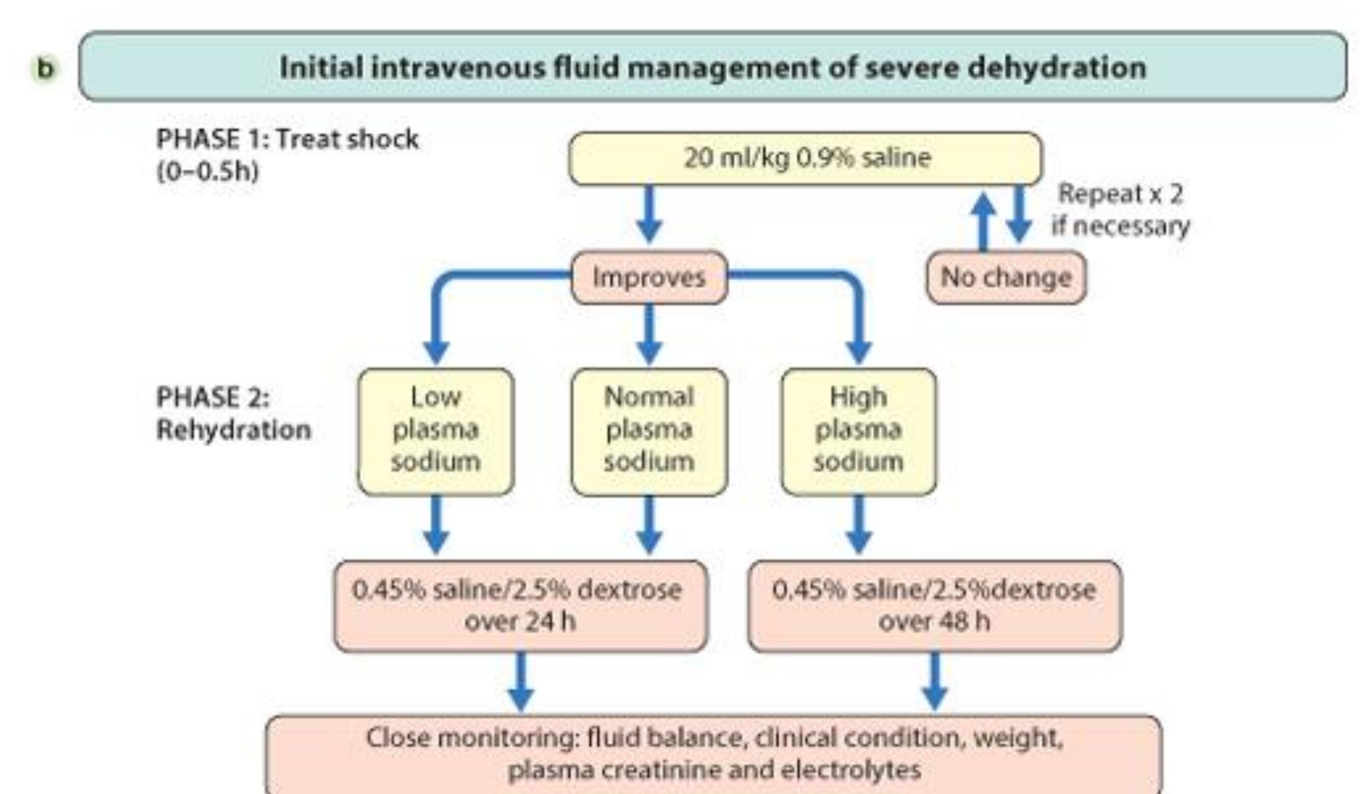
- In such circumstances, a return to an oral rehydration solution for 24 hours, followed by a further introduction of a normal diet, is usually successful.
- Rarely, multiple dietary intolerances may result, such that specialist dietary management is required in the implementation of a diet which excludes cow's milk, disaccharides and gluten.
- In very severe cases, a period of parenteral nutrition is required to enable the injured small intestinal mucosa to recover sufficiently to absorb luminal nutrients

POST-INFECTIVE IRRITABLE BOWEL SYNDROME

Following an episode of gastroenteritis, particularly with a bacterial cause, a substantial proportion of children will develop symptoms of irritable bowel syndrome which may persist for some years. Characteristically, intermittent diarrhoea and abdominal pain (often relieved by defecation) occur, sometimes interspersed with constipation. In between episodes of pain and diarrhoea, affected children are symptom-free, have good general health and grow normally. The condition usually resolves spontaneously. No medication has been shown to be effective, except loperamide for diarrhoea.

Fluid management of severe dehydration





c **Maintenance intravenous fluid requirements**

Body weight	Fluid (ml/kg/24h)	Sodium (mmol/kg/24 h)	Potassium (mmol/kg/24 h)
First 10 kg	100	2–4	1.5–2.5
Second 10 kg	50	1–2	0.5–1.5
Subsequent kg	20	0.5–1	0.2–0.7

For example, the maintenance fluid requirements of a 24 kg child are:
1000 + 500 + 80 = 1580 ml/24 h.

DETAILS OF THE MOST IMPOTANT CAUSES OF NEONATAL CHOLESTASIS

1- Biliary atresia

Pathology :

This occurs in 1 in 14000 live births. It is a progressive disease in which there is destruction or absence of the extrahepatic biliary tree and intrahepatic biliary ducts. This leads to chronic liver failure and death unless surgical intervention is performed.

Clinical presentation :

- Babies with biliary atresia have a normal birthweight but ***fail to thrive*** as the disease progresses.
- They are ***jaundiced*** and from the second day their ***stools are pale and their urine dark***, although both the jaundice and stool colour may fluctuate.
- ***Hepatomegaly*** is present and ***splenomegaly*** will develop secondary to portal hypertension.

Investigations :

- ***Standard liver function tests*** are of little value in the differential diagnosis.
- ***A fasting abdominal ultrasound*** may be normal, or demonstrate a contracted or absent gall bladder.
- ***A radioisotope scan with*** TBIDA (iminodiacetic acid derivatives) shows good uptake by the liver, but no excretion into the bowel.
- ***Liver biopsy*** demonstrates features of extrahepatic biliary obstruction, i.e. fibrosis and proliferation of bile ductules, although there may be features of neonatal hepatitis.
- The diagnosis is confirmed at laparotomy by ***operative cholangiography***, which fails to outline a normal biliary tree.

Treatment :

consists of surgical bypass of the fibrotic ducts, ***hepatoportoenterostomy (Kasai procedure***), in which the jejunum is anastomosed to patent ducts in the cut surface of the porta hepatis. If surgery is performed before the age of 60 days, 80% of children achieve bile drainage. The success rate diminishes with increasing age - hence the need for early diagnosis and treatment.

Postoperative complications include cholangitis and fat malabsorption. Even when bile drainage is successful, there may be progression to cirrhosis and portal hypertension. If the operation is unsuccessful, liver transplantation has to be considered.

2- neonatal hepatitis

CHOLEDOCHAL CYSTS

Definition :

These are cystic dilatations of the extrahepatic biliary system.

Presentation :

About 25% present in infancy with cholestasis. In the older age group, choledochal cysts present with abdominal pain, a palpable mass and jaundice or cholangitis.

The diagnosis :

is established by ultrasound or radionuclide scanning.

Treatment:

is by surgical excision of the cyst with the formation of a roux-en-Y anastomosis to the biliary duct. Future complications include cholangitis and a 2% risk of malignancy, which may develop in any part of the biliary tree.

α1-ANTITRYPSIN DEFICIENCY

Deficiency of the protease α_1-antitrypsin is associated with liver disease in infancy and childhood and emphysema in adults.

Aetiology :

It is inherited as an ***autosomal recessive*** disorder with an incidence of 1 in 2000-4000 in the UK. There are

many phenotypes of the protease inhibitor (Pi) which are coded on chromosome 14. Liver disease is associated with the phenotype PiZZ.

Presentation :

- The majority of babies present ***with prolonged (persistent) neonatal jaundice***,
- but some develop ***bleeding, including intracranial haemorrhage,*** from vitamin K deficiency, particularly if they are breast-fed.
- ***Hepatomegaly*** is present. ***Splenomegaly*** develops with cirrhosis and portal hypertension.

Diagnosis :

The diagnosis is confirmed by estimating the level of α_1-antitrypsin in the plasma and identifying the phenotype.

Treatment and prognosis :

- Approximately 30% of children will recover,
- but the remainder will develop chronic liver disease, some of whom will develop cirrhosis and portal hypertension and require liver transplantation.
- Pulmonary disease is not significant in childhood.
- The disorder can be diagnosed antenatally.

GALACTOSAEMIA

Incidence :

This very rare disorder has an incidence of 1 in 40000.

Presentation :

- The infants develop poor feeding, vomiting, jaundice and hepatomegaly when fed milk.
- Chronic liver failure, cataracts and developmental delay are inevitable if galactosaemia is untreated.
- A rapidly fatal course with shock, haemorrhage and disseminated intravascular coagulation, often due to Gram-negative sepsis, may occur.

Diagnosis :

- ✓ The condition can be screened for in prolonged (persistent) jaundice by detecting galactose, a reducing substance, in the urine.
- ✓ The diagnosis is made by measuring the enzyme galactose-1-phosphate-uridyl transferase in red cells.

Management :

A galactose-free diet prevents progression of liver disease, but ovarian failure and learning difficulties may occur later.

3-Intrahepatic biliary hypoplasia

ALAGILLE'S SYNDROME

is an autosomal dominant condition.
Infants have :

- characteristic triangular facies,
- skeletal abnormalities,
- peripheral pulmonary stenosis,
- renal tubular disorders,
- defects in the eye
- and intrahepatic biliary hypoplasia with severe pruritus and failure to thrive.

Prognosis is variable, with 50% of children surviving into adult life without liver transplantation.

PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS (PFIC)

- is a heterogeneous group of cholestatic disorders of bile acid transporter defects.
- Children present with jaundice, itching, failure to thrive, diarrhoea and a variable progression of liver disease.
- Prognosis is variable, but some children will require liver transplantation.

REYE'S SYNDROME AND REYE-LIKE SYNDROME

Reye's syndrome is an acute non-inflammatory encephalopathy with microvesicular fatty infiltration of the liver. Although the aetiology is unknown, there is a close association with aspirin therapy. Since stopping giving aspirin to children aged less than 12 years, Reye's syndrome has virtually disappeared. With the introduction of tandem mass spectroscopy in the neonatal screening programme, the commonest beta oxidation defect, medium chain acyl-CoA dehydrogenase deficiency (MCAD), is diagnosed early in many regions of the UK. Many of these patients would have presented with acute liver failure and a Reye-like syndrome later in life.

DETAILS OF SOME CAUSES OF CHRONIC LIVER DISEASE

Cystic fibrosis

Pathology :

Abnormal bile acid concentration and biliary disease is seen in cystic fibrosis as the CFTR (cystic fibrosis transmembrane regulator) is found in biliary epithelial cells.

Presentation :

Cirrhosis and portal hypertension develop in 20% of children by mid-adolescence.

Diagnosis :

Early liver disease is difficult to detect by biochemistry, ultrasound or radioisotope scanning. Liver histology includes fatty liver, focal biliary fibrosis or focal nodular cirrhosis.

Management :

Therapy includes standard supportive and nutritional therapy with ursodeoxycholic acid. Liver transplantation should be considered for those with end-stage liver disease, either alone or in combination with a heart-lung transplant.

Congenital hepatic fibrosis

- Congenital hepatic fibrosis (CHF) presents in children over 2 years old with hepatosplenomegaly, abdominal distension and portal hypertension. Renal disease may coexist.
- Congenital hepatic fibrosis differs from cirrhosis in that liver function tests are normal in the early stage. Liver histology shows large bands of hepatic fibrosis containing abnormal bile ductules.
- The consequent portal hypertension causes bleeding from varices.

Non-alcoholic fatty liver disease

- Non-alcoholic fatty liver disease (NAFLD) is diagnosed in up to 60% of overweight children but it can also be found in lean individuals and in certain metabolic syndromes.
- The term NAFLD includes benign fatty infiltration of the liver as well as more aggressive forms with inflammation and fibrosis that may progress to cirrhosis in childhood.
- The pathogenesis is not understood but may be linked to insulin resistance. In obese children liver function tests improve with weight loss.

NUTRITIONAL SUPPORT OF CHILD WITH LIVER DISEASE

Malnutrition may be due to protein malnutrition, fat malabsorption, anorexia or fat-soluble vitamin deficiency (vitamins A, D, E and K).

Protein & carb :

Treatment is to provide a high-protein except if he is susceptible to encephalopathy , high-carbohydrate diet with 50% more calories than the recommended dietary allowance.

Fat :

- In children with cholestasis, medium-chain triglycerides, which are absorbed by the portal circulation,

will provide fat, but 20-40% long-chain triglycerides are required to prevent essential fatty acid deficiency.

- Many children will require nasogastric tube feeding or parenteral nutrition

vitamins :

- **Vitamin K deficiency** in liver disease may be due to malabsorption or diminished synthesis. ***Water-soluble forms of vitamin K are available***.
- **Vitamin A deficiency** causes night blindness in adults and retinal changes in infants. It is easily prevented ***with oral vitamin A*** .
- **Vitamin E deficiency cau**ses peripheral neuropathy, haemolysis and ataxia. It is very poorly absorbed in cholestatic conditions and ***high oral doses are required***.
- **Vitamin D deficiency causes** rickets and pathological fractures. It is prevented by using a water-soluble form of vitamin D. Vitamin D-resistant rickets indicates renal tubular acidosis.

LIVER TRANSPLANTATION

Liver transplantation is accepted therapy for acute or chronic end-stage liver failure and has revolutionised the prognosis for these children. Transplantation is also considered for some hepatic malignancy.

The indications for transplantation in chronic liver failure are:

- severe malnutrition unresponsive to intensive nutritional therapy
- recurrent complications (bleeding varices, resistant ascites)
- failure of growth and development
- poor quality of life.

Liver transplant evaluation includes

- assessment of the vascular anatomy of the liver
- and exclusion of irreversible disease in other systems.
- Absolute contraindications include
  - sepsis,
  - untreatable cardiopulmonary disease
  - cerebrovascular disease.

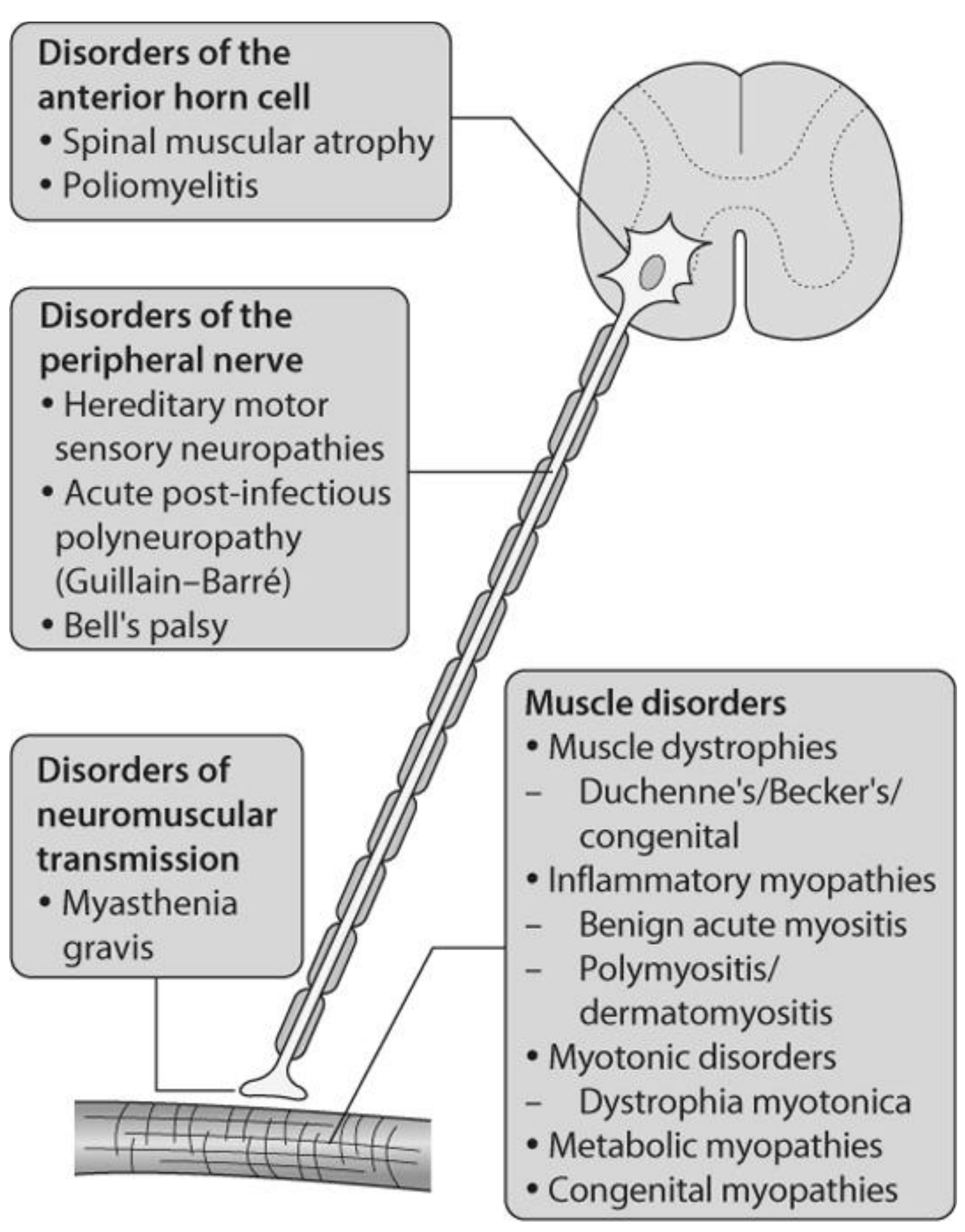
There is considerable difficulty in obtaining small organs for children. Most children receive part of an adult's liver, which is either reduced to fit the child's abdomen (reduction hepatectomy) or split (shared between an adult and child).

Complications post-transplantation include:

- primary non-function of the liver (5%)
- hepatic artery thrombosis (10-20%)
- biliary leaks and strictures (20%)
- rejection (30-60%)
- sepsis, the main cause of death.

In large national centres, the overall 1-year survival is approximately 90%, and the overall 5-year survival is more than 80%. Most deaths occur in the first 3 months. Children who survive the initial postoperative period usually do well. Long-term studies indicate normal psychosocial development and quality of life in survivors.

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THE HEREDITARY MOTOR SENSORY NEUROPATHIES (HMSN)

- This group of disorders typically leads to symmetrical, slowly progressive muscular wasting which is distal rather than proximal.
- Type I, formerly known as peroneal muscular atrophy (Charcot-Marie-Tooth disease), is usually dominantly inherited and the most common.
- Affected nerves may be hypertrophic due to demyelination followed by attempts at remyelination.
- Nerve biopsy typically shows 'onion bulb formation' due to these two processes. Onset is in the first decade with distal atrophy and pes cavus, the legs being affected more than the arms. Rarely, there may be distal sensory loss and the reflexes are diminished. The disease is chronic and only rarely do those affected lose the ability to walk. The initial presentation of Friedreich's ataxia can be similar.

BELL'S PALSY

Bell's palsy is an isolated lower motor neuron paresis of the VIIth cranial nerve leading to facial weakness . Although the aetiology is unclear in Bell's palsy, it is probably post-infectious with an association with herpes simplex virus in adults. Corticosteroids may be of value in reducing oedema in the facial canal during the first week. Recovery is complete in the majority of cases but may take several months. The main complication is conjunctival infection due to incomplete eye closure on blinking. This may require the eye to be protected with a patch or even tarsorrhaphy.

There are several other causes of facial nerve palsy.

- If symptoms of an VIIIth nerve paresis are also present then the most likely diagnosis is a compressive lesion in the cerebellopontine angle.
- The herpes virus may invade the geniculate ganglion and give painful vesicles on the tonsillar fauces and external ear, along with a facial nerve paresis. Treatment for this is with aciclovir.
- Hypertension should be excluded, as there is an association between Bell's palsy and coarctation of the aorta.
- If the facial weakness is bilateral, sarcoidosis should be suspected, but this is also seen in Lyme disease.

JUVENILE MYASTHENIA

Aetiology : This is similar to adult autoimmune myasthenia and is due to binding of antibody to acetylcholine receptors on the post-junctional synaptic membrane. This gives a reduction of the number of functional receptors.
Presentation is usually after 10 years of age with ophthalmoplegia and ptosis, loss of facial expression and difficulty chewing (Fig. 27.15). Generalised, especially proximal, weakness may be seen

Diagnosis is made by observing improvement following the administration of intravenous edrophonium and can be further confirmed by testing for acetylcholine receptor antibodies (seen in 60-80%).

Treatment is with

- the use of anti-cholinesterases such as neostigmine or pyrido-stigmine. In the longer term,
- immunosuppressive therapy with prednisolone or azathioprine has been shown to be of value.
- Plasma exchange is used for crises.
- Thymectomy is considered if a thymoma is present or if the response to medical therapy is unsatisfactory. About a quarter will show remission post thymectomy and up to half show some improvement.

MANAGEMENT OF DUCHENNE MUSCULAR DYSTROPHY

- Appropriate exercise helps to maintain muscle power and mobility and delays the onset of scoliosis.
- Contractures, particularly at the ankles, should be prevented by passive stretching and the provision of night splints.
- Walking can be prolonged with the provision of orthoses, in particular those which allow ambulation by the child leaning from side to side.

- Lengthening of the Achilles tendon may be required to facilitate ambulation.
- Attention to maintaining a good sitting posture helps to minimise the risk of scoliosis.
- Scoliosis is managed with a truncal brace, a moulded seat and occasionally surgical insertion of a metal rod into the spine.
- Later in the illness, episodes of nocturnal hypoxia secondary to weakness of the intercostal muscles may present with lassitude or irritability. Respiratory aids, particularly overnight CPAP (continuous positive airway pressure) or non-invasive positive pressure ventilation (NIPPV), may be provided to improve the quality of life.
- As with all chronic disabling conditions, parent self-help groups are a useful continuing source of information and support for families. Affected children should be reviewed periodically at a specialist regional centre.
- Ambulant children with Duchenne's dystrophy are increasingly treated with corticosteroids (prednisolone for 10 days per month) to preserve mobility and prevent scoliosis. The precise mechanism by which glucocorticoids may increase strength in Duchenne's dystrophy is not known but their potential beneficial effects include
    - inhibition of muscle proteolysis,
    - a stimulatory effect on myoblast proliferation,
    - an increase in myogenic repair, an anti-inflammatory/immunosuppressive effect,
    - reduction of cytosolic calcium concentrations and upregulation of utrophin,
    - and alteration in skeletal muscle gene expression.

METABOLIC MYOPATHIES

Metabolic conditions can affect muscles, due either to the deposition of storage material or to energy-depleting enzyme deficiencies. Presentation is as a floppy infant or, in older children, with muscle weakness or cramps on exercise. The main causes are:

- Glycogen storage disorders .
- Disorders of lipid metabolism. Fatty acids are important muscle fuel. Fatty acid oxidation occurs in the mitochondria and defects in this pathway can result in weakness. Carnitine is essential to supply long-chain fatty acids to the mitochondria for breakdown, and carnitine deficiency causes weakness.
- Mitochondrial cytopathies - rare disorders which are coded as maternally inherited mitochondrial DNA. Myopathy may be the major manifestation or the disorder may be multisystem, with lactic acidosis and encephalopathy. Mitochondrial DNA testing is available.

CONGENITAL MYOPATHIES

These present at birth or in infancy with generalised hypotonia and muscle weakness. The names describe the changes seen on muscle biopsy or electron microscopy. They include:

- nemaline rod myopathy
- central core disease
- congenital fibre-type disproportion.

Creatine phosphokinase levels are normal or only mildly elevated.



Vesicoureteric reflux

DEFINITION : Vesicoureteric reflux (VUR) is a developmental anomaly of the vesicoureteric junctions. The ureters are displaced laterally and enter directly into the bladder rather than at an angle, with a shortened or absent intramural course. Severe cases may be associated with renal dysplasia.

AETIOLOGY AND INCIDENCE : It is familial, with a 30-50% chance of occurring in first-degree relatives. It may also occur with bladder pathology, e.g. a neuropathic bladder or urethral obstruction, or temporarily after a UTI.

PATHOPHYSIOLOGY : Its severity varies from reflux into the lower end of an undilated ureter during micturition to the severest form with reflux during bladder filling and voiding, with a distended ureter, renal pelvis and clubbed calyces . Mild reflux is unlikely to be of significance, but the more severe degrees of VUR may be associated with *intrarenal reflux* (IRR), the backflow of urine from the renal pelvis into the papillary collecting ducts; IRR is associated with a particularly high risk of renal scarring if UTIs occur. The incidence of renal defects increases with increasing severity of reflux; however, many children with renal defects do not have reflux. With growth, reflux resolves in 10% each year.

Reflux with associated ureteric dilatation is important, as:

- urine returning to the bladder from the ureters after voiding results in incomplete bladder emptying, which encourages infection
- the kidneys may become infected (pyelonephritis), particularly if there is intrarenal reflux
- bladder voiding pressure is transmitted to the renal papillae; this may contribute to renal damage if voiding pressures are high.

COMPLICATIONS : Infection may destroy renal tissue, leaving a scar, resulting in a shrunken, poorly functioning segment of kidney (reflux nephropathy). If scarring is bilateral and severe, chronic renal failure may develop. The risk for hypertension in childhood or early adult life is variously estimated to be up to 10%.

Follow-up of children with recurrent UTIs, renal scarring or reflux

In these children:

- Urine culture should be checked with a non-specific illness in case it is caused by a UTI (urine should not be cultured routinely).
- Long-term low-dose antibiotic prophylaxis can be used. There is no evidence for when antibiotic prophylaxis should be stopped. Consideration should be at the age of 2 years (by when maximum renal growth has occurred) or after 1 year free of UTIs.
- Circumcision in boys may be considered as there is evidence that it reduces the incidence of urinary tract infection.
- Anti-reflux surgery may be indicated if there is progression of scarring with ongoing reflux, but it has not been shown to improve outcome.
- Blood pressure should be checked annually if renal defects are present.
- Regular assessment of renal growth and function is necessary if there are bilateral defects because of the risk of chronic renal failure.

If there are further symptomatic UTIs in younger children, investigations are required to determine whether

there are new scars or continuing reflux. New scars are rare in previously unscarred kidneys after 4 years of age, even in the presence of continuing VUR, and reinvestigation is rarely indicated after this age.

DAYTIME ENURESIS

AETIOLOGY ; This is a lack of bladder control during the day in a child old enough to be continent (over the age of 3-5 years). Nocturnal enuresis is also usually present. It may be caused by:

- lack of attention to bladder sensation, a manifestation of a developmental or psychogenic problem which may be secondary to stress or part of a general behavioural problem, although it may occur in otherwise normal children who are too preoccupied with what they are doing to respond to the sensation of a full bladder
- detrusor instability (uncoordinated bladder contractions)
- bladder neck weakness
- a neuropathic bladder
- a urinary tract infection (although rarely in the absence of other symptoms)
- constipation
- an ectopic ureter.

EXAMINATION may reveal :

- evidence of a neuropathic bladder, i.e. the bladder may be distended,
- there may be abnormal perineal sensation and anal tone
- abnormal leg reflexes and gait.
- Sensory loss in the distribution of the S2, 3 and 4 dermatomes should be sought.
- A spinal lesion may be present.
- Girls who are dry at night but wet on getting up are likely to have pooling of urine from an ectopic ureter opening into the vagina.

INVESTIGATIONS :

- A urine sample is examined for microscopy, culture and sensitivity. Other investigations are performed if indicated.
- An ultrasound may show bladder pathology, with incomplete bladder emptying or thickening of the bladder wall.
- Urodynamic studies may be required.
- An X-ray of the spine may reveal a vertebral anomaly.
- An MRI scan may be required to confirm or exclude a non-bony spinal defect such as tethering of the cord.

TREATMENT :

Affected children in whom a neurological cause has been excluded may benefit from

- star charts, bladder training and pelvic floor exercises.
- Constipation should be treated.
- A small portable alarm with a pad in the pants, which is activated by urine, can be used when there is lack of attention to bladder sensation.
- Anticholinergic or adrenergic drugs, such as oxybutynin to damp down bladder contractions or ephedrine to increase tone at the bladder neck, may be helpful if other measures fail.

HENOCH-SCHÖNLEIN PURPURA

DEFINITION :

Henoch-Schönlein purpura is the combination of:

- characteristic skin rash
- arthralgia
- periarticular oedema
- abdominal pain
- glomerulonephritis.

INCIDENCE :

It usually occurs between the ages of 3 and 10 years, is twice as common in boys, peaks during the winter months and is often preceded by an upper respiratory infection.

AETIOLOGY :

Despite much research, the cause is unknown. It is postulated that genetic predisposition and antigen exposure increase circulating IgA levels and disrupt IgG synthesis. The IgA and IgG interact to produce complexes that activate complement and are deposited in affected organs, precipitating an inflammatory response with vasculitis.

CLINICAL FINDINGS

At presentation, affected children often have a fever.

1- ***The rash*** is the most obvious feature.
   a. It is symmetrically *distributed over the buttocks*, the extensor surfaces of the arms and legs, and the ankles. The trunk is spared unless lesions are induced by trauma.
   b. The rash may initially be *urticarial*, rapidly becoming *maculopapular* and purpuric, is *characteristically palpable* and may recur over several weeks.
   c. The rash is the first clinical feature in about 50% and is the cornerstone of the diagnosis, which is clinical.
2- ***Joint pain*** occurs in two-thirds of patients, particularly of the knees and ankles. There is *periarticular oedema*. Long-term damage to the joints does not occur, and symptoms usually resolve before the rash goes.
3- ***Colicky abdominal pain*** occurs in many children and, if severe, can be treated with corticosteroids.
   a. Gastrointestinal petechiae can cause haematemesis and melaena. Intussusception can occur and can be particularly difficult to diagnose under these circumstances.
   b. Ileus, protein-losing enteropathy, orchitis and occasionally central nervous system involvement are rare complications.
4- ***Renal involvement*** is common, but is rarely the first symptom.
   a. Over 80% have microscopic or macroscopic haematuria or mild proteinuria. These children usually make a complete recovery.
   b. If proteinuria is more severe, nephrotic syndrome may result. Risk factors for progressive renal disease are heavy proteinuria, oedema, hypertension and deteriorating renal function, when a renal biopsy will determine if treatment is necessary.
   c. All children with renal involvement are followed for a year to detect those with persisting urinary abnormalities (5-10%) who require long term follow-up. This is necessary as hypertension and declining renal function may develop after an interval of several years

HAEMOLYTIC URAEMIC SYNDROME

. **Haemolytic uraemic syndrome (HUS) - the triad of:**

- **acute renal failure**
- **haemolytic anaemia**
- **thrombocytopenia.**

The pathophysiology of the disorder is not well understood; it is thought to be due to activation of neutrophils which damage vascular endothelium. Typical HUS is secondary to gastrointestinal infection with verocytotoxin-producing *E. coli* O157:H7 or, less often, *Shigella*. It follows a prodrome of bloody diarrhoea.

Although the platelet count is reduced, the clotting is normal (unlike in disseminated intravascular coagulation, DIC). Other organs such as the brain, pancreas and heart may also be involved.

Treatment :

With early supportive therapy, including dialysis, the **typical diarrhoea**-associated HUS usually has a good prognosis, although follow-up is necessary as there may be persistent proteinuria and the development of hypertension and declining renal function in subsequent years.

In contrast, **atypical HUS** has no diarrhoeal prodrome, may be familial and frequently relapses. It has a high risk of hypertension and chronic renal failure and has a high mortality.

Children with intracerebral involvement or with atypical HUS may be treated with prostacyclin or plasma exchange, but their efficacy is unproven.

DIABETES

Problems in diabetic control

Good blood glucose control is particularly difficult in the following circumstances:

- *Eating too many sugary foods*, such as sweets taken at odd times, at parties or on the way home from school.
- *Infrequent or unreliable blood glucose testing*. 'Perfect' results are often invented and written down just before clinic to please the diabetes team.
- *Illness - viral illnesses are common in the young and although it is usually stated that infections cause insulin requirements to increase*, in practice the insulin dose required is variable, partly because of reduced food intake. The dose of insulin should be adjusted according to regular blood glucose monitoring. Insulin *must* be continued during times of illness and the urine or blood tested for ketones. If ketosis is increasing along with a rising blood sugar, the family should know how to seek immediate advice to ensure that they increase the soluble insulin dose appropriately or seek medical help for possible intravenous therapy.
- *Exercise - vigorous or prolonged planned exercise* (cross-country running, long-distance hiking, skiing) requires reduction of the insulin dose and increase in dietary intake. Late hypoglycaemia may occur during the night or even the next day, but may be avoided by taking an extra bedtime snack, including slow-acting carbohydrate such as cereal or bread. Less vigorous exercise such as sports lessons in school and spontaneous outdoor play can be managed with an extra snack or a reduction in short-acting insulin before the exercise.
- *Family disturbance* such as divorce or separation.
- *Inadequate family motivation*, support or understanding. As children can never have a 'holiday' from their diabetes, they need a great deal of encouragement to continuously maintain good control. Educational programmes for children and families need to be arranged regularly and matched to their current level of education. Special courses and holiday camps are available; in the UK they are organised by Diabetes UK and local groups

How diabetes interferes with normal adolescence

Aims and problems of normal adolescence	**How diabetes interferes**
Physical and sexual maturation	Delayed sexual maturation Invasion of privacy with frequent medical examinations
Conformity with peer group	Meals must be eaten on time Frequent injections and blood tests
Self-image	Hypoglycaemic attacks show that they are different
Self-esteem	Impaired body image
Independence from parents	Parental over-protection and reluctance to allow their child to be away from home Battles over diabetes
Economic independence	Loading of insurance premiums Discrimination by employers Statutory rules against becoming a pilot or driving heavy goods or public service vehicles

Assessment of the child with diabetes

Assessment of diabetic control:

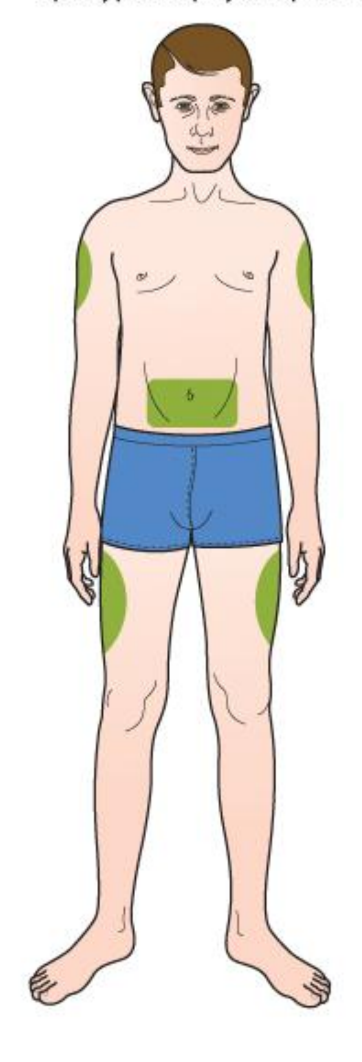
- Any episodes of hypoglycaemia, diabetic ketoacidosis, hospital admission?
- Absence from school
- Interference with normal life
- HbA_{1c} results
- Diary of blood glucose results – if monitoring, is he reacting to results?
- Insulin regimen – appropriate?
- Diet – healthy diet, manipulating food intake and insulin to maintain good control?

General overview (periodic):

- Normal growth and pubertal development, avoiding obesity
- Blood pressure check for hypertension
- Renal disease – screening for microalbuminuria
- Eyes – for retinopathy or cataracts
- Feet – maintaining good care
- Screening for coeliac and thyroid disease
- Annual reminder to have flu vaccination

Knowledge and psychosocial aspects:

- Good understanding of diabetes, would participation/ holidays with other diabetic children be beneficial? Member of Diabetes UK?
- Becoming self-reliant, but appropriate supervision at home, school, diabetic team?
- Taking exercise, sport? Diabetes not interfering with it?
- Leading as normal life as possible?
- Smoking, alcohol?
- Is 'hypo' treatment readily available?
- Are there short-term goals to improve control?



Developmental Milestones

When considering developmental milestones:

- **The *median age*** is the age when half of a standard population of children achieve that level; it serves as a guide to when stages of development are likely to be reached but does not tell us if the child's skills are outside the normal range.
- ***Limit ages*** are the age by which they should have been achieved. Limit ages are usually 2 standard deviations from the mean. They are more useful as a guide to whether a child's development is normal than the median ages. Failure to meet them gives guidance for action regarding more detailed assessment, investigation or intervention.

The difference between median and limit ages can be demonstrated by considering the age range for the important developmental milestone of walking unsupported. The percentage of children who take their first steps unsupported is:

- 25% by 11 months
- 50% by 12 months
- 75% by 13 months
- 90% by 15 months
- 97.5% by 18 months.

The median age is 12 months and is a guide to the common pattern to expect, although the age range is wide. The limit age is 18 months (two standard deviations from the mean). Of those not achieving the limit age, many will be normal late walkers, but a proportion will have an underlying medical problem, such as cerebral palsy, a primary muscle disorder or global developmental delay. A few may be understimulated from social deprivation. Hence, any child who is not walking by 18 months should be assessed and examined. Thus 18 months can be set as a 'limit age' for children not walking. Setting the limit age earlier may allow earlier identification of problems, but will also increase the number of children labelled as 'delayed' who are in fact normal.

Cognitive Development

Cognition refers to higher mental function. This progresses with age. In infancy, thought processes are centred around immediate experiences. **The thought processes of preschool children** (which have been called preoperational thought by Piaget), tend to be:

- that they are the centre of the world
- that inanimate objects are alive and have feelings and motives
- that events have a magical element
- that everything has a purpose. Toys and other objects are used in imaginative play as aids to thought to help make sense of experience and social relationships.

In middle school children, the dominant mode of thought is practical and orderly, tied to immediate circumstances and specific experiences. (This has been called operational thought.)

It is only **in the mid-teens** that an adult style of abstract thought (formal operational thought) begins to develop, with the ability for abstract reasoning, testing hypotheses and manipulating abstract concepts

Mahmoud Behairy

MAIN STAGES OF DEVELOPMENT

Age	Gross motor	Vision and fine motor	Hearing and speech and language	Social, emotional and behavioural
Newborn	Flexed posture	Fixes and follows face	Stills to voice Startles to loud noise	Smiles - only at 6 weeks
7 months	Sits without support	Transfers objects from hand to hand	Turns to voice Polysyllabic babble	Finger feeds Fears strangers
1 year	Stands independently	Pincer grip 10 months Points	1-2 words Understands name	Drinks from cup Waves
18 months	Walks independently	Immature grip of pencil Random scribble	6-10 words Points to 4 body parts	Feeds himself with spoon Beginning to help with dressing
2½ years	Runs and jumps	Draws	3-4 word sentences Understands 2 joined commands	Parallel play Clean and dry

PRESENTATION OF NEURODEVELOPMENTAL CONCERNS BY AGE

Prenatal	Positive family history, e.g. affected siblings or family members; ethnicity, e.g. Tay-Sachs disease in Jewish parents
	Antenatal screening tests, e.g. ultrasound for spina bifida or hydrocephalus, amniocentesis for Down's syndrome
Perinatal	Following birth asphyxia/neonatal encephalopathy
	Preterm infants with intraventricular haemorrhage/periventricular leucomalacia, post haemorrhagic hydrocephalus
	Dysmorphic features
	Abnormal neurological behaviour - tone, feeding, movement, seizures, visual inattention
Infancy	Global developmental delay
	Delayed or asymmetric motor development
	Visual or auditory concerns by parent or after screening
	Neurocutaneous/dysmorphic features
Preschool	Speech and language delay
	Abnormal gait
	Loss of skills
School age	Problems with balance and coordination
	Learning difficulties
	Attention control
	Hyperactivity
	Specific learning difficulties, e.g. dyslexia, dyspraxia
Any age	Acquired brain injury, e.g. after meningitis, head injury

Edwards' syndrome (trisomy 18) and Patau's syndrome (trisomy 13)

Although rarer than Down's syndrome (1 in 8000 and 1 in 14 000 live births, respectively), particular constellations of severe multiple abnormalities suggest the diagnosis at birth and most affected babies die in infancy .

The diagnosis is confirmed by chromosome analysis. Many affected fetuses are detected by ultrasound scan during the second trimester of pregnancy and diagnosis can be confirmed antenatally by amniocentesis and chromosome analysis.

Recurrence risk is low, except when the trisomy is due to a balanced chromosome rearrangement in one of the parents.

Clinical features of Edwards' syndrome (trisomy 18)

- Low birthweight
- Prominent occiput
- Small mouth and chin
- Short sternum
- Flexed, overlapping fingers
- Rocker-bottom feet
- Cardiac and renal malformations

Clinical features of Patau's syndrome (trisomy 13)

- Structural defect of brain
- Scalp defects
- Small eyes (microphthalmia) and other eye defects
- Cleft lip and palate
- Polydactyly
- Cardiac and renal malformations

Chromosomal abnormalities

RECIPROCAL TRANSLOCATIONS

An exchange of material between two different chromosomes is called a reciprocal translocation.
When this exchange involves no loss or gain of chromosomal material, the translocation is 'balanced' and has no phenotypic effect if not it is unbalanced.
Balanced reciprocal translocations are relatively common, occurring in 1 in 500 of the general population. A translocation that appears balanced on conventional chromosome analysis may still involve the loss of a few genes or the disruption of a single gene that results in an abnormal phenotype, often including learning difficulty. Studying the chromosomal breakpoints in such individuals has been one way of identifying the location of specific genes.
Unbalanced reciprocal translocations contain an incorrect amount of chromosomal material and cause a combination of dysmorphic features, congenital malformations, developmental delay and learning difficulties. In a newborn baby, the prognosis is difficult to predict, but the effect is usually severe. The parents' chromosomes should be checked to determine whether the abnormality has arisen de novo, or as a consequence of a parental rearrangement. Finding a balanced translocation in one parent indicates a recurrence risk for future pregnancies and antenatal diagnosis by chorionic villus sampling or amniocentesis should be offered as well as testing of relatives.

DELETIONS

Deletions are another type of structural abnormality. Loss of part of a chromosome usually results in physical abnormalities and learning difficulties. The deletion may involve loss of the terminal or, less commonly, the interstitial part of a chromosome.

An example of a deletion syndrome involves loss of the tip of the short arm of chromosome 5, hence the name 5p- or monosomy 5p. Because affected babies have a high-pitched mewing cry in early infancy, it is also known as *cri du chat* syndrome. Parental chromosomes should be checked to see if one parent carries a balanced chromosomal rearrangement.

An increasing number of syndromes are now known to be due to chromosome deletions too small to be seen by conventional cytogenetic analysis. These submicroscopic deletions can be detected by FISH (fluorescent in-situ hybridisation) studies using DNA probes specific to particular chromosome regions. DiGeorge's syndrome is due to a deletion of chromosome 22 at band 22q11 . Williams' syndrome is another example of a microdeletion syndrome due to loss of chromosomal material on the long arm of chromosome 7 at band 7q11 .

NO FAMILY HISTORY OF THE DISORDER IN AUTOSOMAL DOMINANT GENES

May be due to:

- A new mutation in one of the gametes leading to the conception of the affected person. This is the most common reason for absence of a family history in dominant disorders, e.g. >80% of individuals with achondroplasia have normal parents.
- Gonadal mosaicism - very occasionally a healthy parent harbours the mutation only in a number of gametes in the gonad. This can account for recurrences of autosomal dominant disorders in siblings born to apparently normal parents. It has been described in congenital lethal osteogenesis imperfecta.
- Non-paternity - if the apparent father is not the biological father.

DNA ANALYSIS

New techniques in DNA testing are continually being developed, making more single gene disorders amenable to molecular analysis. Most molecular testing is performed using polymerase chain reaction (PCR). This involves the amplification of specific DNA sequences, enabling rapid analysis of small samples, which is particularly important in antenatal diagnosis.
The main impact of DNA analysis for genetic counselling is:

- confirmation of a clinical diagnosis
- detection of female carriers in X-linked disorders, e.g. Duchenne's and Becker's muscular dystrophies, haemophilia A and B
- carrier detection in autosomal recessive disorders, e.g. cystic fibrosis
- presymptomatic diagnosis in autosomal dominant disorders, e.g. Huntington's disease, myotonic dystrophy
- antenatal diagnosis of an increasing number of Mendelian conditions.

These are accomplished by:

- **1. Mutation analysis**
  For an increasing number of disorders, it is possible to directly detect the actual mutation causing the disease. This provides very accurate results for confirmation of diagnosis, and presymptomatic or

predictive testing. Identifying the mutation in an affected individual may be very time-consuming, but once this has been done, testing other relatives is usually fairly simple. Examples are:

- **Deletions** - large deletion mutations are common in a variety of disorders including *Duchenne's and Becker's muscular dystrophies, alpha-thalassaemia and 21-hydroxylase deficiency* (congenital adrenal hyperplasia). They can be tested for relatively easily.
- **Point mutations** and small deletions - these can be readily identified if the same mutation causes all cases of the disorder, as in sickle cell disease. For most disorders, however, there is a very diverse spectrum of mutations. About 78% of cystic fibrosis carriers in the UK possess the ΔF508 mutation, but over 900 other mutations have been identified. Most laboratories test for a certain number of the most common mutations in their given population.
- **Trinucleotide repeat expansion mutations** - these are readily tested for because the mutation in a given disease is always the same. The only difference is the size of the repeat sequence, which can be determined from the size of the DNA fragment containing the repeat.

- **2. Genetic linkage**
  If mutation analysis is not available, it may be possible to use DNA sequence variations (markers) located near to, or within, the disease gene to track the inheritance of this gene through a family. This type of analysis requires a suitable family structure and several key members need to be tested to identify appropriate markers before linkage testing can be used predictively

PRESYMPTOMATIC TESTING

In many autosomal dominant disorders, onset is during adolescence or adult life and clinical expression may not be evident at birth. Relatives of affected individuals may request tests to see if they are likely to develop the disorder in question. Examples include myotonic dystrophy, Huntington's disease, autosomal dominant polycystic kidney disease and neurofibromatosis.
Assessment may include:

- careful examination of individuals at risk, e.g. development of café-au-lait patches and axillary freckling in neurofibromatosis
- investigations, e.g. renal ultrasound scans in individuals at risk of autosomal dominant polycystic kidney disease
- DNA analysis using linked markers or mutation analysis.

It is generally accepted that presymptomatic tests (e.g. for Huntington's disease and myotonic dystrophy) and carrier tests (e.g. for cystic fibrosis) should not be performed on healthy children, as these remove the child's future right to choose whether or not to have this information.

DYSMORPHOLOGY

The term 'dysmorphology' literally means 'the study of abnormal form' and refers to the assessment of birth defects and unusual physical features that have their origin during embryogenesis.

PATHOGENIC MECHANISMS

Malformation
A primary structural defect occurring during the development of a tissue or organ, e.g. spina bifida and cleft lip and palate.

Deformation
Implies an abnormal intrauterine mechanical force that distorts a normally formed structure, e.g. joint contractures due to fetal compression caused by severe oligohydramnios.

Disruption
Involves destruction of a fetal part which initially formed normally; e.g. amniotic membrane rupture may lead to amniotic bands which may cause limb reduction defects.

Dysplasia
Refers to abnormal cellular organisation or function of specific tissue types, e.g. skeletal dysplasias and dysplastic kidney disease

CLINICAL CLASSIFICATION OF BIRTH DEFECTS

Single-system defects

These include single congenital malformations such as spina bifida and are often multifactorial in nature with fairly low recurrence risks.

Sequence

Refers to a pattern of multiple abnormalities occurring after one initiating defect. Potter's syndrome (fetal compression and pulmonary hypoplasia) is an example of a sequence in which all abnormalities may be traced to one original malformation, renal agenesis.

Association

A group of malformations that occur together more often than expected by chance, but in different combinations from case to case, e.g. VACTERL association (Vertebral anomalies, Anal atresia, Cardiac defects, Tracheo-oEsophageal fistula, Renal anomalies, Limb defects).

Syndrome

When a particular set of multiple anomalies occurs repeatedly in a consistent pattern, this is called a 'syndrome'. Multiple malformation syndromes are often associated with moderate or severe learning difficulties and may be due to:

- chromosomal defects
- a single gene defect (dominant or recessive)
- exposure to teratogens such as alcohol, drugs (especially anticonvulsants such as valproate, carbamazapine and phenytoin) or viral infections during pregnancy
- unknown cause.

CLINICAL FEATURES OF NOONAN'S SYNDROME

- Characteristic facies
- Occasional mild learning difficulties
- Short webbed neck with trident hair line
- Pectus excavatum
- Short stature
- Congenital heart disease (especially pulmonary stenosis, atrial septal defect)

CLINICAL FEATURES OF WILLIAMS' SYNDROME

- Short stature
- Characteristic facies
- Transient neonatal hypercalcaemia (occasionally)
- Congenital heart disease (supravalvular aortic stenosis)
- Mild to moderate learning difficulties

CLINICAL FEATURES OF PRADER-WILLI SYNDROME

- Characteristic facies
- Hypotonia
- Neonatal feeding difficulties
- Failure to thrive in infancy
- Obesity in later childhood
- Hypogonadism
- Developmental delay
- Learning difficulties

Maternal conditions affecting the fetus

Diabetes

Women with insulin-dependent diabetes *find it more difficult to maintain* good diabetic control during pregnancy and have an increased insulin requirement.
Poorly controlled maternal diabetes is associated with polyhydramnios and pre-eclampsia, increased rate of early fetal loss, congenital malformations and late unexplained intrauterine death.
Ketoacidosis carries a high fetal mortality. With meticulous attention to diabetic control, the perinatal mortality rate is now only slightly greater than in non-diabetics.
Fetal problems associated with maternal diabetes are:

- ***Congenital malformations***. Overall, there is a 6% risk of congenital malformations, a threefold increase compared with the non-diabetic population. The range of anomalies is similar to that for the general population, apart from an increased incidence of cardiac malformations, sacral agenesis (caudal regression syndrome) and hypoplastic left colon, although the latter two conditions are rare. Studies show that good diabetic control periconceptionally reduces the risk of congenital malformations.
- ***Intrauterine growth restriction (IUGR)***. There is a threefold increase in growth restriction in mothers with long-standing microvascular disease.
- ***Macrosomia*** (Fig. 9.4). Maternal ***hyperglycaemia*** causes fetal hyperglycaemia as glucose crosses the placenta. As insulin does not cross the placenta, the fetus responds with increased secretion of insulin which promotes growth by increasing both cell number and size. About 25% of such infants have a birthweight greater than 4 kg compared with 8% of non-diabetics. The macrosomia predisposes to cephalopelvic disproportion, birth asphyxia, shoulder dystocia and brachial plexus injury.

Neonatal problems include:

- ***Hypoglycaemia.*** Transient hypoglycaemia is common during the first day of life from fetal hyperinsulinism, but can often be prevented by early feeding. The infant's blood glucose should be closely monitored during the first 24 hours and hypoglycaemia treated.
- ***Respiratory distress syndrome (RDS)***. More common as lung maturation is delayed.
- ***Hypertrophic cardiomyopathy***. Hypertrophy of the cardiac septum occurs in some infants. It regresses over several weeks but may cause heart failure from reduced left ventricular function.
- ***Polycythaemia*** (venous haematocrit >0.65). Makes the infant look plethoric. Treatment with partial exchange transfusion to reduce the haemocrit and normalise viscosity may be required.

Maternal medication which may adversely affect the fetus

Medication	Adverse effect
Anticonvulsant therapy with carbamazepine , valproic acid (sodium valproate) or hydantoins (phenytoin)	Fetal carbamazepine/valproate/hydantoin syndrome - midfacial hypoplasia, CNS, limb and cardiac malformations, developmental delay.
Cytotoxic agents	Congenital malformations
Diethylstilbestrol (DES)	Clear-cell adenocarcinoma of vagina and cervix
Iodides/propylthiouracil	Goitre, hypothyroidism
Lithium	Congenital heart disease
Tetracycline	Enamel hypoplasia of the teeth

Thalidomide	Limb shortening (phocomelia)
Vitamin A and retinoids	Increased spontaneous abortions, abnormal face
Warfarin	Interferes with cartilage formation (nasal hypoplasia and epiphyseal stippling); cerebral haemorrhages and microcephaly

CONGENITAL INFECTIONS

Intrauterine infection is usually from maternal primary infection during pregnancy. Those that can damage the fetus are:

- rubella
- cytomegalovirus (CMV)
- *Toxoplasma gondii*
- parvovirus
- varicella zoster
- syphilis.

RUBELLA

The diagnosis of maternal infection must be confirmed serologically as clinical diagnosis is unreliable. The risk and extent of fetal damage are mainly determined by the gestational age at the onset of maternal infection.

- **Infection before 8 weeks'** gestation causes deafness, congenital heart disease and cataracts in over 80% .
- About 30% of fetuses of mothers **infected at 13-16 weeks'** gestation have impaired hearing;
- **beyond 18 weeks'** gestation the risk to the fetus is minimal.
- Viraemia after birth continues to damage the infant..

Congenital rubella is preventable. In the UK, it has become rare since the measles/mumps/rubella (MMR) vaccine was introduced into the childhood immunisation programme, but this is dependent on the maintenance of a high vaccine uptake rate.

CYTOMEGALOVIRUS

CMV is **the most common** congenital infection, affecting 3-4/1000 live births in the UK, with higher rates reported in parts of the USA.

- In Europe, **50%** of pregnant women are **susceptibl**e to CMV.
- About 1% of susceptible women will have a **primary infection during pregnancy**,and in about 40% of them the **infant becomes infected**.
- The infant may also become infected following **recurrent infection in a pregnant woman who is immune**, but this is much less likely to damage the fetus.

When an infant is infected:

- 90% are normal at birth and **develop normally**
- 5% have **clinical features at birth**, such as hepatosplenomegaly and petechiae , most of whom will have neurodevelopmental disabilities such as sensorineural hearing loss, cerebral palsy, epilepsy and cognitive impairment
- 5% develop **problems later in life**, mainly sensorineural hearing loss.

TOXOPLASMOSIS

Mode of transmission :

Acute infection with *Toxoplasma gondii*, a protozoan parasite, may result from the consumption of raw or undercooked meat and from contact with the faeces of recently infected cats. In the UK, fewer than 20% of pregnant women have had past infection, in contrast to 80% in France and Austria.

Transmission to fetus :

Transplacental infection may occur during the parasitaemia of a primary infection, and about 40% of fetuses become infected.

Symptoms :

Most infected infants are asymptomatic. About 10% have clinical manifestations , of which the most common are:

- retinopathy, an acute fundal chorioretinitis which sometimes interferes with vision
- cerebral calcification
- hydrocephalus.
- These infants usually have long-term neurological disabilities.
- Asymptomatic infants remain at risk of developing chorioretinitis into adulthood.

Diagnosis :

- ***Serological diagnosis :*** As the specific IgM antibody test has a low sensitivity, serial IgG antibody tests are needed to differentiate passively acquired maternal antibody from fetal infection.
- ***Amniocentesis :*** Confirmation of fetal infection is obtained from amniocentesis
- ***U/S :*** The severely affected fetus may also have evidence on ultrasound of a fetal anomaly, e.g. hydrocephalus or cerebral calcification, but these can only be recognised at advanced gestation

Treatment :

- Women who show seroconversion can be treated with the antibiotic spiromycin.
- If positive amniocentesis, treatment with the pyrimethamine and sulfadiazine or termination of pregnancy can be offered.
- Infected newborn infants are treated for a year.

VARICELLA ZOSTER

Incidence an drisk of infection : Fifteen per cent of pregnant women are susceptible to varicella (chickenpox). Usually, the fetus is unaffected but will be at risk if the mother develops chickenpox:

- ***in the first half of pregnancy*** (<20 weeks), when there is a <2% risk of the fetus developing severe scarring of the skin and possibly ocular and neurological damage and digital dysplasia
- ***within 5 days before or 2 days after delivery***, when the fetus is unprotected by maternal antibodies and the viral dose is high. About 25% develop a vesicular rash. The illness has a mortality as high as 30%.

Protection ;Exposed susceptible women can be protected with varicella zoster immune globulin (VZIG) and treated with aciclovir. Infants born in the high-risk period should also receive zoster immune globulin and are often also given aciclovir prophylactically.

SYPHILIS :

Congenital syphilis is rare in the UK. The clinical features are shown in. Those specific to congenital syphilis include a characteristic rash on the soles of the feet and hands and bone lesions. If mothers with syphilis identified on antenatal screening are fully treated a month or more before delivery, the infant does not require treatment and has an excellent prognosis. If there is any doubt about the adequacy of maternal treatment, the infant should be treated with penicillin.

DIAGNOSIS OF CONGENITAL RUBELLA, CYTOMEGALOVIRUS (CMV) AND TOXOPLASMA INFECTION

Mother	Seroconversion on screening serology
Fetus	Amniocentesis or chorionic villus sample - PCR
Placenta	Microscopy for syphilis, PCR
Urine from infant	Rubella, CMV - culture, PCR
Blood, CSF, other samples from infant	Culture, PCR
Blood serology	Rubella-specific IgM CMV-specific IgM *Toxoplasma*-specific IgM and persistently raised *Toxoplasma* IgG

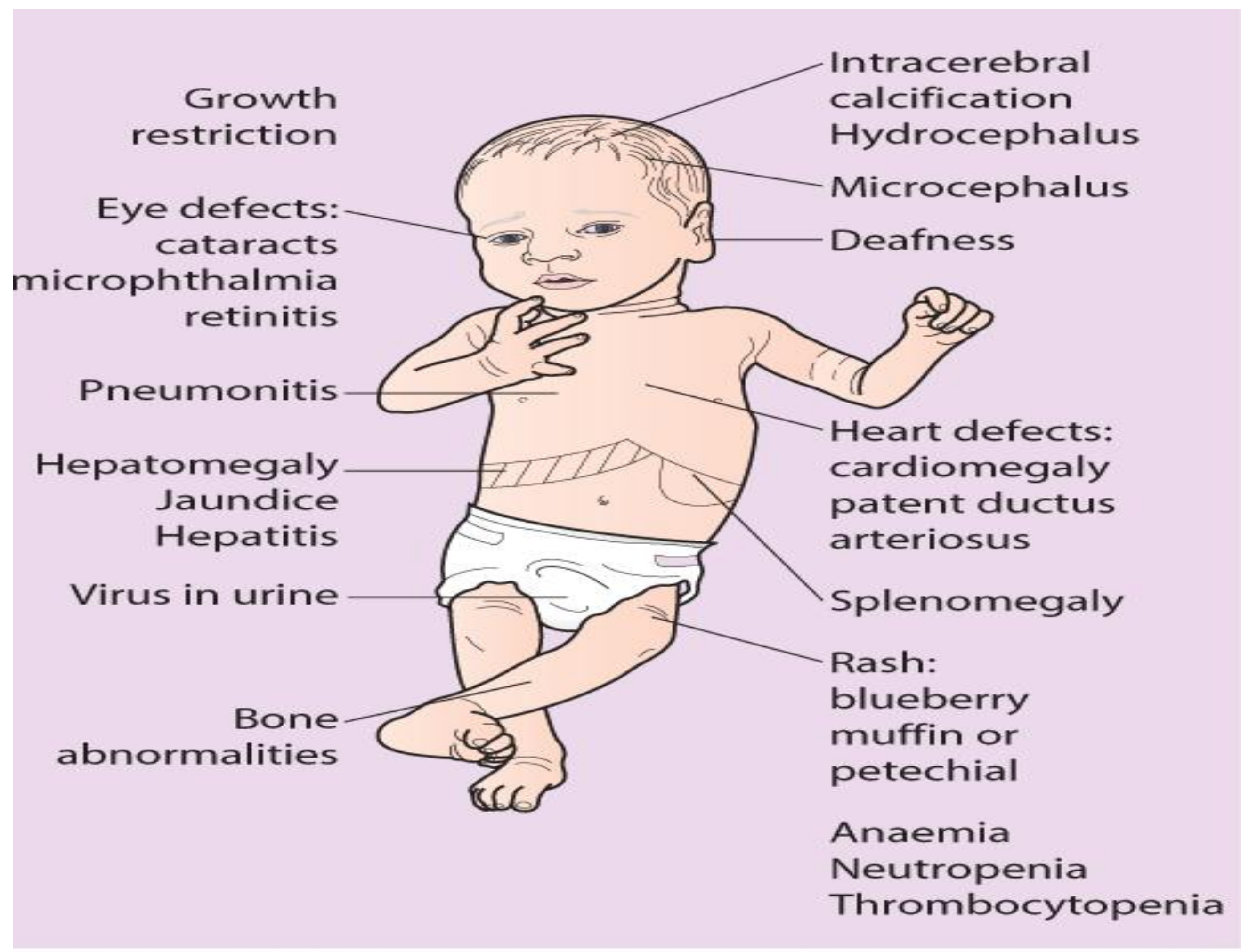


Figure 9.6b Clinical features of congenital rubella, cytomegalovirus (CMV), toxoplasmosis and syphilis

PATTERNS OF GROWTH RESTRICTIONS

Growth restriction in both the fetus and infant has traditionally been classified as symmetrical or asymmetrical.

Asymmetrical growth :

In the more common asymmetrical growth restriction, the weight or abdominal circumference lies on a lower centile than that of the head. This occurs when the placenta fails to provide adequate nutrition late in pregnancy but brain growth is relatively spared at the expense of liver glycogen and skin fat (Fig. 9.11). This form of growth restriction is associated with uteroplacental dysfunction secondary to maternal pre-eclampsia, multiple pregnancy, maternal smoking, or it may be idiopathic. These infants rapidly put on weight after birth

Symmetrical growth :

In symmetrical growth retardation, the head circumference is equally reduced. It suggests a prolonged period of poor intrauterine growth (or that the gestational age is incorrect). It is usually due to a small but normal fetus, but may be due to a fetal chromosomal disorder or syndrome, a congenital infection, maternal drug and alcohol abuse or a chronic medical condition or malnutrition. These infants are more likely to remain small permanently.
In practice, distinction between asymmetrical and symmetrical growth restriction often cannot be made

SOME MEDICAL PROBLEMS IN NEONATES

PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN

Clinical features :

This life-threatening condition is usually associated with :

1. Birth asphyxia, meconium aspiration, septicaemia or ***respiratory distress syndrome***. It sometimes occurs as a primary disorder.
2. As a result of the high pulmonary vascular resistance, there is right-to-left shunting within the lungs and at atrial and ductal levels. ***Cyanosis occurs soon after birth***.
3. Heart murmurs and signs of heart failure are often absent.

Investigations :

1. *A chest X-ray* shows that the heart is of normal size and there may be pulmonary oligaemia.
2. *An urgent echocardiogram* is required to establish that the child does not have congenital heart disease.

Treatment :

1. Most infants require ***mechanical ventilation and circulatory support*** in order to achieve adequate oxygenation.
2. ***Inhaled nitric oxide*** , a potent vasodilator, is often beneficial.
3. Another vasodilator, ***sildenafil***, has been introduced more recently.
4. High-frequency or ***oscillatory ventilation*** is sometimes helpful.
5. Extracorporeal membrane oxygenation ***(ECMO)***, where the infant is placed on heart and lung bypass for several days, is indicated for severe cases, but is only performed in a few specialist centres.

Mahmoud Behairy

DIAPHRAGMATIC HERNIA

Clinical presentation :

- ✓ It usually presents with ***failure to respond to resuscitation*** or as respiratory distress.
- ✓ In most cases there is a left-sided herniation of abdominal contents through the posterolateral foramen of the diaphragm. The apex beat and heart sounds will then be ***displaced to the right side*** of the chest, with ***poor air entry in the left chest***.
- ✓ Vigorous resuscitation may cause a ***pneumothorax in the normal lung***, thereby aggravating the situation.

Investigations : The diagnosis is confirmed by ***X-ray*** of the chest and abdomen . Many are now diagnosed on antenatal ultrasound screening

Management :

- ✓ Once the diagnosis is suspected, a ***large nasogastric tube*** is passed and suction is applied to prevent distension of the intrathoracic bowel.
- ✓ After stabilisation, the diaphragmatic hernia is ***repaired surgically***
- ✓ but in most infants with this condition the main problem is ***pulmonary hypoplasia*** - where compression by the herniated viscera throughout pregnancy has prevented development of the lung in the fetus. If the lungs are hypoplastic, mortality is high.
- ✓ ***ECMO*** has been used pre- and postoperatively to provide respiratory support

HYPOGLYCAEMIA

Causes :

Hypoglycaemia is particularly likely to occur in the first 24 hours of life in:

- ➢ babies who had intrauterine growth restriction,***IUGR*** (poor glycogen stores)
- ➢ who are ***preterm*** (poor glycogen stores)
- ➢ born to mothers with ***diabetes mellitus*** (have sufficient glycogen stores, but hyperplasia of the islet cells in the pancreas causes high insulin levels)
- ➢ are ***large-for-dates***, hypothermic
- ➢ ***polycythaemic*** or ill for any reason. h whereas the infants of a diabetic mother.

Symptoms :

are jitteriness, irritability, apnoea, lethargy, drowsiness and seizures.

Diagnosis :

There is no agreed definition of hypoglycaemia in the newborn. Many babies tolerate low blood glucose levels in the first few days of life, as they are ***able to utilise lactate and ketones as energy stores***. Recent evidence suggests that blood glucose ***levels above 2.6 mmol/L*** are desirable for optimal neurodevelopmental outcome, although during the first 24 hours after birth many asymptomatic infants transiently have blood glucose levels below this level. There is good evidence that prolonged, symptomatic hypoglycaemia can ***cause permanent neurological disability***.

Management :

Hypoglycaemia can usually be prevented by early and frequent milk feeding.
In infants at increased risk of hypoglycaemia, blood glucose is regularly ***monitored at the bedside***.

- If an asymptomatic infant has two low glucose values (i.e. below 2.6 mmol/L) in spite of adequate

feeding

- or one very low value (<1.6 mmol/L)
- or becomes symptomatic

- glucose is given by intravenous infusion aiming to maintain the glucose >2.6 mmol/L. The concentration of the intravenous dextrose may need to be increased from 10% to 15% or even 20%. Abnormal blood glucose results should be confirmed in the laboratory. High concentration intravenous infusions of glucose should be given via a central venous catheter to avoid extravasation into the tissues, which may cause skin necrosis and reactive hypoglycaemia.
- If there is difficulty or delay in starting the infusion, or a satisfactory response is not achieved, glucagon or hydrocortisone can be given.

GASTROINTESTINAL DISORDERS

Oesophageal atresia

Incidence :

Oesophageal atresia is usually associated with a tracheo-oesophageal fistula . It occurs in 1 in 3500 live births and is associated with polyhydramnios during pregnancy.

Clinical presentation :

If not diagnosed at birth, clinical presentation is with:

1. persistent salivation and drooling from the mouth after birth,
2. associated with choking and cyanotic episodes.

If the diagnosis is not made at this stage,

- ✓ the infant will cough and choke when fed.
- ✓ There may be aspiration into the lungs of saliva (or milk) from the upper airways and acid secretions from the stomach.

Almost half of the babies have other congenital malformation, e.g. as ***part of the VACTERL association*** (Vertebral, Anorectal, Cardiac, Tracheo-oEsophageal, Renal and Radial Limb anomalies).

Invetigations :

1. In oesophageal atresia, If suspected, a wide-calibre feeding tube is passed and checked to see if it reaches the stomach.
2. a chest X-ray will confirm that a wide-calibre feeding tube has failed to reach the stomach.

   Continuous suction is applied to the tube to reduce aspiration of saliva and secretions pending transfer to a neonatal surgical unit.

Small bowel obstruction

Clinical presentation :

This may be recognised antenatally on ultrasound scanning. Otherwise, small bowel obstruction presents with :

- ***persistent vomiting***, which is bile-stained unless the obstruction is above the ampulla of Vater.
- Meconium may initially be passed, but subsequently its passage is usually ***delayed or absent***.
- ***Abdominal distension*** becomes increasingly prominent the more distal the bowel obstruction.
- High lesions will present soon after birth, but lower obstruction may not present for some days.

Causes :

Small bowel obstruction may be caused by:

- ***atresia or stenosis of the duodenum*** - a third have Down's syndrome and it is also associated with other congenital malformations
- ***atresia or stenosis of the jejunum or ileum*** - there may be multiple atretic segments of bowel
- ***malrotation with volvulus*** - a dangerous condition as it may lead to infarction of the entire midgut
- ***meconium ileus*** - thick inspissated meconium, of putty-like consistency, becomes packed into the lower ileum; almost all affected neonates have cystic fibrosis
- ***meconium plug*** - a plug of inspissated meconium causes lower intestinal obstruction.

Diagnosis :

The diagnosis is made on clinical features and ***abdominal X-ray*** showing intestinal obstruction.

Management :

Atresia or stenosis of the bowel and malrotation are treated surgically, after correction of fluid and electrolyte depletion. ***A meconium plug*** will usually pass spontaneously. ***Meconium ileus*** may be dislodged using Gastrografin contrast medium.

Large bowel obstruction

This may be caused by:

- ***Hirschsprung's disease***. Absence of the myenteric nerve plexus in the rectum which may extend along the colon. The baby often does not pass meconium within 48 hours of birth and subsequently the abdomen distends. About 15% present as an acute enterocolitis .
- ***Rectal atresia***. Absence of the anus at the normal site. Lesions are high or low, depending whether the bowel ends above or below the levator ani muscle. In high lesions there is a fistula to the bladder or urethra in boys, or the vagina or bladder in girls. Treatmnt is surgical.

Exomphalos/gastroschisis

In exomphalos (also called omphalocele), the abdominal contents protrude through the umbilical ring, covered with a transparent sac formed by the amniotic membrane and peritoneum . It is often associated with other major congenital abnormalities.

In gastroschisis the bowel protrudes through a defect in the anterior abdominal wall, adjacent to the umbilicus, and there is no covering sac . It is not associated with other congenital abnormalities.

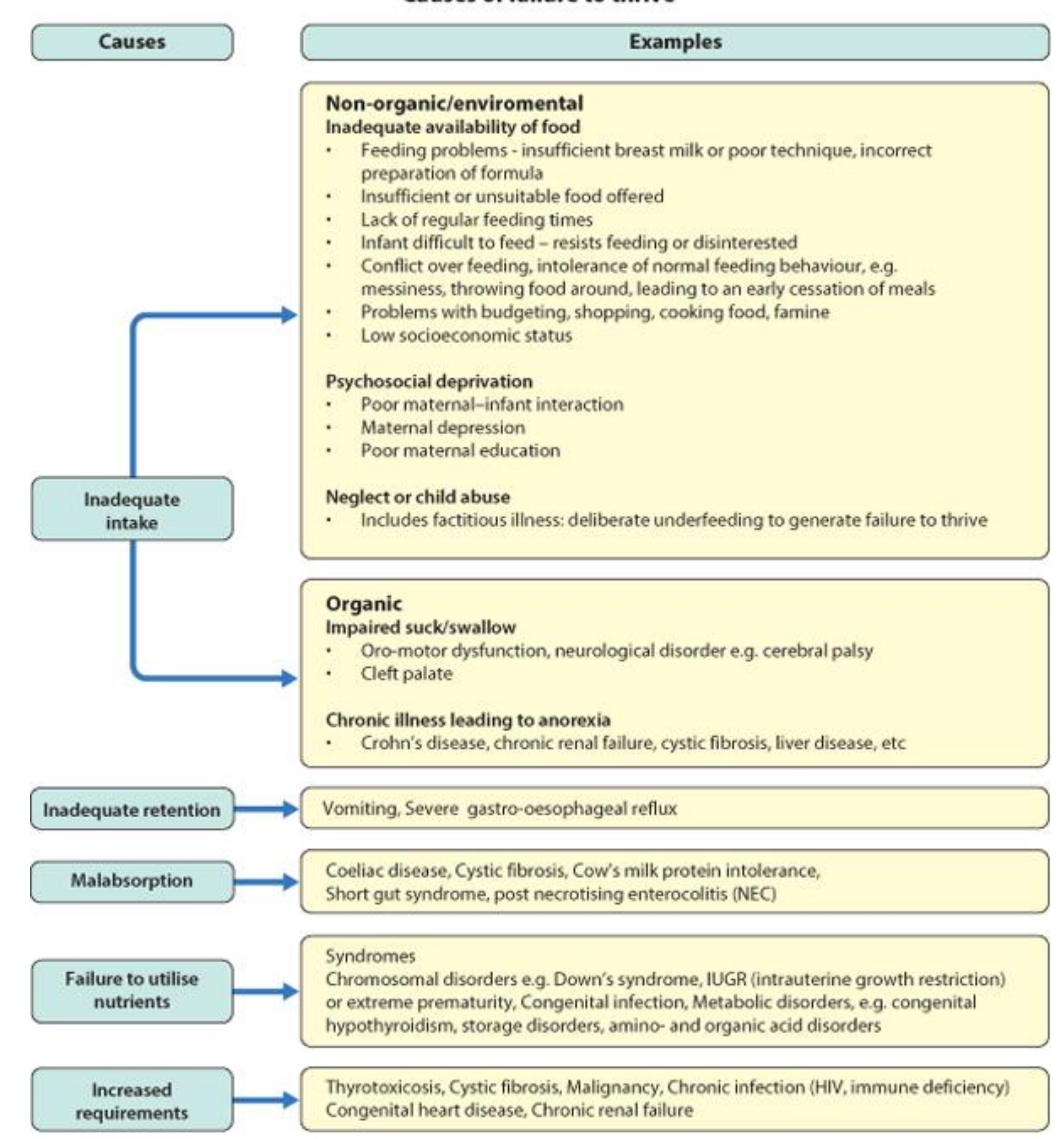
Complications :

Gastroschisis carries a much greater risk **of dehydration** and **protein loss**, so the abdomen of affected infants should be wrapped in several layers of clingfilm to minimise fluid and heat loss.

Management :

- ☒ **A nasogastric tube** is passed and aspirated frequently
- ☒ an intravenous infusion **of dextrose** established.
- ☒ **Colloid** support is often required to replace protein loss.
- ☒ Many lesions can be repaired by **primary closure of the abdomen**. With large lesions, the intestine is enclosed in a silastic sac sutured to the edges of the abdominal wall and the contents gradually returned into the peritoneal cavity.

FAILURE TO THRIVE



Clinical features

Studying the growth chart in combination with the history and examination of the child is the key to its evaluation. The history should focus on:

- a detailed **dietary history**; a food diary over a few days can be informative
- **feeding**, including details of exactly what happens at mealtimes
- if the child is well and has lots of energy or has other symptoms such as diarrhoea, vomiting, cough, lethargy
- if the child was **premature** or had intrauterine growth restriction at birth or any significant medical problems
- the growth of **other family members** and any illnesses in the family
- if the child's **development** is normal
- if there are **psychosocial problems at home**.

Examination focuses on identifying whether there is any evidence of organic disease

- - dysmorphic features, distended abdomen, thin buttocks and irritability in coeliac disease,
- respiratory signs and malabsorption in cystic fibrosis,
- evidence of nutritional deficiencies or evidence of chronic illness.

investigations

Investigations to be considered in failure to thrive

Investigation	Significance of an abnormality
Full blood count and differential	Anaemia, infection, inflammation, immune deficiency
Plasma creatinine and electrolytes	Renal failure, renal tubular acidosis, metabolic disorders
Liver function tests	Liver disease, malabsorption, metabolic disorders
Thyroid function tests	Congenital hypothyroidism
Acute-phase reactant	Inflammation, e.g. Crohn's disease
Ferritin	Iron deficiency anaemia
Immunoglobulins	Immune deficiency
Anti-endomysial and anti-gliadin antibodies	Coeliac disease
Urine microscopy and culture and dipsticks	Urinary tract infection, renal disease
Stool microscopy and culture	Intestinal infection, parasites
Karyotype in girls	Turner's syndrome
Chest X-ray and sweat test	Cystic fibrosis

Management

The management of most non-organic failure to thrive is multidisciplinary and is carried out in primary care. **The health visitor** is well placed to make home visits to assess eating behaviour and provide support. Direct practical advice following observation may well be beneficial. **A paediatric dietician** may be helpful in assessing the quantity and composition of food intake, and recommending strategies for increasing energy intake and a **speech and language therapist** has specialist skills with feeding disorders. Input from a clinical psychologist and from social services may also be appropriate. **Nursery placement** may be helpful in alleviating stress at home and assist with feeding.

Hospital admission may occasionally be necessary for a period of assessment and observation of the child and family, or when detailed investigations are required.

Outcome

Follow-up studies suggest that children with non-organic failure to thrive continue to under-eat . Although there is usually a gradual improvement in the preschool years, a lasting deficit is common and these children tend to remain underweight. In contrast, impairment of development is only short term.

Prevention

Prevention of failure to thrive is an essential part of the management of any child whose condition severely affects sucking and swallowing, such as prematurity, cleft palate, oesophageal malformation and cerebral palsy when a gastrostomy may be required to maintain reasonable nutrition.
In children who are unable to tolerate gastric feeding because of severe illness or multiple bowel operations, total parenteral nutrition (TPN) is needed to prevent malnutrition, but is accompanied by increased risk of infection.

ASSESSMENT OF NUTRITIONAL STATUS

Malnutrition must be recognised and accurately defined for rational decisions to be made about refeeding. Evaluation is divided into assessment of past and present dietary intake, anthropometry and laboratory assessments.

Dietary assessment

Parents are asked to record as best they can all food the child eats during several days. This gives a reasonably accurate assessment of habitual food intake. Children under 12 years are likely to give unreliable information if questioned directly

Anthropometry

Regular growth measurements are valuable as a fall-off of a growth parameter is one of the earliest indicators of incipient malnutrition. Height, weight, triceps skinfold thickness and mid-arm circumference are basic measures which permit a reasonably accurate assessment of nutritional status. The World Health Organization recommends that nutritional status is expressed as:

- ***height for age*** - a measure of stunting and an index of chronic malnutrition
- ***weight for height*** - a measure of wasting and an index of acute malnutrition .

Subcutaneous fat stores can be assessed by measuring skinfold thickness, whilst ***upper arm circumference*** in conjunction with triceps skinfold thickness is an indication of skeletal muscle mass. However, it is difficult to measure skinfold thickness accurately in young children, so this reduces its use in reflecting short-term changes in body composition.

Laboratory investigations

These are useful in the detection of early physiological adaptation to malnutrition, but clinical history, examination and anthropometry are of greater value than any single biochemical or immunological measurement.

CYTOMEGALOVIRUS (CMV)

Mode of transmiddion

Cytomegalovirus is usually transmitted via saliva, genital secretions or breast milk, and more rarely via blood products, organ transplants and transplacentally.

Incidence

The virus causes ***mild or subclinical infection*** in normal hosts. In developed countries, about ***half of the adult*** population show serological evidence of past infection. In developing countries, most children have been infected by 2 years of age, often ***via breast milk***. In the immunocompromised and the fetus, CMV is an important pathogen.

Presentation :

- As with EBV, CMV may cause a ***mononucleosis syndrome***. Pharyngitis and lymphadenopathy are not usually as prominent as in EBV infections. Patients may have atypical lymphocytes on the blood film but are heterophile antibody-negative.
- Maternal CMV infection may result in ***congenital infection*** (see Ch. 9), which may be present at birth or develop when older.
- In the ***immunocompromised host***, CMV can cause retinitis, pneumonitis, bone marrow failure, encephalitis, hepatitis, colitis and oesophagitis. It is a very important pathogen following organ transplantation. Organ recipients are closely monitored for evidence of CMV activation by sensitive tests such as polymerase chain reaction (PCR).

Prevention

Interventions used to reduce the risk of transmission of CMV disease are CMV-negative blood for transfusions and anti-CMV drug prophylaxis; also, if possible, CMV-positive organs are not transplanted into CMV-negative recipients. CMV disease may be treated with ganciclovir or foscarnet, but both have serious side-effects

HUMAN HERPESVIRUS 7 (HHV7)

This virus is very closely related to HHV6, causing similar clinical disease, including exanthem subitum(reseola infantum) and febrile convulsions. Again, most children are infected with HHV7 in the first few years of life.

HUMAN HERPESVIRUS 8 (HHV8)

This virus is associated with ***Kaposi's sarcoma (KS)***, a tumour which occurs in ***immunosuppressed*** patients as well as certain populations in Africa and around the Mediterranean. HHV8 does not appear to be associated with disease in otherwise healthy children. Primary HHV8 infection may be associated with a ***mild febrile illness***, and infection is usually transmitted from ***saliva***. Up to 40% of African teenagers have ***antibodies to HHV8***, whereas <5% are seropositive in the UK.

PARVOVIRUS B19

Disease :

Parvovirus B19 ***causes erythema infectiosum or fifth disease*** (so-named because it was the fifth disease to be described of a group of illnesses with similar rashes), also called slapped cheek syndrome.

Incidence :

Infections can occur at any time of the year, although outbreaks are most common during the *spring months*.

Mode of transmission

Transmission is via *respiratory secretions* from viraemic patients, by *vertical transmission* from mother to fetus and by transfusion of *contaminated blood products*. Parvovirus B19 infects the erythroblastoid red cell precursors in the bone marrow.

Clinical presentation

Parvovirus causes a range of clinical syndromes:

- *asymptomatic infection* - common; about 5-10% of preschool children and 65% of adults have antibodies
- *erythema infectiosum* - the most common illness,
  - with a viraemic phase of fever, malaise, headache and myalgia
  - followed by a characteristic rash a week later on the face ('slapped cheek'), progressing to a maculopapular, 'lace'-like rash on the trunk and limbs
  - complications are rare in children, although arthralgia or arthritis is common in adults
- *aplastic crisis* - the most serious consequence of parvovirus infection; it occurs in children with chronic haemolytic anaemias, where there is an increased rate of red cell turnover (e.g. sickle cell disease or thalassaemia); and in immunodeficient children (e.g. malignancy) who are unable to produce an antibody response to neutralise the infection
- *fetal disease* - transmission of maternal parvovirus infection may lead to fetal hydrops and death due to severe anaemia, although the majority of infected fetuses will recover.

ENTEROVIRUSES

Organisms :

Human enteroviruses, of which there are many (including the coxsackie viruses, echoviruses and polio viruses), are a common cause of childhood infection.

Transmission

is primarily by the faecal-oral route. Following replication in the pharynx and gut, the virus spreads to infect other organs.

Incidence :

Infections occur most commonly in the summer and autumn.

Presentations :

Over 90% of infections are asymptomatic or cause a non-specific febrile illness, but characteristic clinical syndromes exist and are listed below. An effective vaccine is available against the polioviruses.

The following may be caused by enteroviruses:

HERPANGINA

Vesicular and ulcerated lesions on the soft palate and uvula causing anorexia, pain on swallowing and fever.

HAND, FOOT AND MOUTH DISEASE

Painful vesicular lesions on the hands, feet, mouth and tongue. Systemic features are mild. The disease subsides within a few days.

MENINGITIS/ENCEPHALITIS

Aseptic meningitis is caused by many of the enteroviruses. There may be a skin rash, which can be petechial and therefore difficult to differentiate clinically from meningococcal infection. Complete recovery can be expected.

Pleurodynia (Bornholm's disease)

An acute illness with fever, pleuritic chest pain and muscle tenderness. There may be a pleural rub but examination is otherwise normal. Recovery is within a few days.

Myocarditis and pericarditis

Heart failure associated with a febrile illness and ECG evidence of myocarditis.

Poliovirus infection

Clinical disease is now very rare, due to successful immunisation programmes. It falls into four main categories:

- >90% are asymptomatic
- 5% have a poliomyelitis 'minor illness' - fever, headache, malaise, sore throat and vomiting occur within 4 days of exposure and recovery is uneventful
- 2% of patients progress to central nervous system involvement with aseptic meningitis; there is stiffness of the back, neck and hamstrings from meningeal irritation
- in <1% of cases, classical paralytic polio occurs about 4 days after the minor illness has subsided - involvement of the anterior horn cells and cerebral cortex leads to varying degrees of paralysis which may recover completely or be permanent; involvement of the muscles of respiration may call for long-term respiratory support or be fatal.

Infection in the immunocompromised host

Enteroviruses can cause severe disease in immunocompromised individuals. Echovirus can cause a persistent and sometimes fatal central nervous system infection in agammaglobulinaemic patients.

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